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CALCIUM AND PHOSPHORUS METABOLISM*

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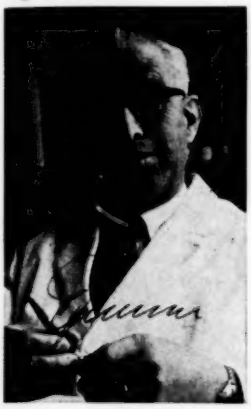
The bones contain more than 99% of the entire calcium of the body (1,200 g. in the adult). The intracellular fluid is completely free of calcium and there is only 0·9 g. in the extracellular fluid. Approximately 6 mg. of the 10 mg. per 100 ml. of total serum calcium are ionized and highly active; 3 - 4 mg. are protein-bound and about 0·5 mg. is found as a complex-salt, bound to citric acid and other organic acids.



Professor Fanconi

The effect of the 6 mg. per 100 ml. of calcium ions in the serum as electrolyte is completely negligible (3 mEq./l.Ca^{++}), whereas Na^{+} represents 140 mEq./l., but this small quantity of calcium is most important in the maintenance of several biological functions. These include neuromuscular excitability, autonomic balance, cardiac function (Ca - K antagonism), blood coagulation, cellular and capillary permeability, antigen-antibody reactions, complement-fixation, and phagocytosis by leucocytes.

The optimum range of calcium concentration for these biological reactions is extremely narrow and must be kept at a very constant level. In childhood it varies between 9·4 and 10·2 mg. per 100 ml. (after Elkington and Danowski), in the younger adult between 9·4 and 10·2 mg. per 100 ml. and in the older adult between 9·6 and 11·0 mg. per 100 ml. This constancy is astonishing when we consider that the total calcium which is absorbed, stored and excreted, has to pass the 'bottle neck' of serum calcium of about 10 mg. per 100 ml. The activity of calcium metabolism varies according to the body's requirements; in spite of this the organism succeeds in keeping the serum-calcium level constant. For instance, radioactive calcium-45 injected intravenously disappears from the blood in less than 1 minute (Hansard, Comar and Davis).

The phosphate concentration in the serum fluctuates much more. It varies between 7·0 mg. per 100 ml. in the newborn and less than 4 mg. per 100 ml. in the adult. It varies also with the season; in spring it is higher than in winter. The inorganic phosphorus determined in the serum by the method of Bell and Doisy exists entirely in the ionized form. Whereas even minor variations in the calcium level cause severe symptoms (hypocalcaemic tetany and hypercalcaemic intoxication), the phosphate level can range from 1·0 to 15 mg. per 100 ml. without causing any symptoms. The control of the phosphate level is done by the kidneys; when the glomeruli are inefficient, hyperphosphataemia will occur; when the tubules are not able to reabsorb phosphates hypophosphataemia will result.

The bones are not only a frame tissue, they also have a very important exchange function. In the iso-ionic exchange calcium and phosphate ions are precipitated in or withdrawn from the bone; in the hetero-ionic exchange other ions like sodium, carbonate, citrate, etc. are exchanged against calcium and phosphate. We know that one-third of the body sodium is bound in an inactive state (dry retention) in the skeleton; in acute cases of sodium-depletion so many calcium ions may be bound in the bones to permit the release of sodium that a hypocalcaemic tetany may occur (personal observation).

Citrate, too, plays an important rôle in the iso-ionic exchange; variations in the concentration of citrate ions in the intracellular fluid of the bones are probably the cause of calcification or decalcification of the matrix.

CONTROL OF SERUM CALCIUM

Considering the severity of the disturbances caused by variations in the level of serum calcium, we must conclude that very accurate mechanisms of control exist. The first, and most rapid one, is in the serum itself; it is the exchange between calcium ions and protein-bound calcium, which follows the mass law. The second mechanism is the iso-ionic exchange between serum and bone. It can only raise the calcium level to 6 mg. per 100 ml.

To increase the serum calcium to the normal level of 10 mg. per 100 ml., a third and more powerful but slowly-acting mechanism, the action of the parathyroids, is necessary. The parathormone has a double function; it stimulates the osteoclasts, so that calcium and phosphate ions are mobilized; furthermore it inhibits the reabsorption of phosphate in the renal tubules. The final result of this double function is the transfer of calcium from the bones into the serum and of phosphate from the bones into the urine. The fourth mechanism of control is the intestinal absorption of calcium; it is increased by vitamin D and decreased by cortisone. In this respect cortisone is an antagonist to vitamin D. The fifth mechanism is the renal excretion probably depending on the level of complexed calcium.

The mode of action of vitamin D is not completely known. Its main functions are believed to be as follows:

Primary functions: Control of intestinal absorption of calcium and phosphorus; transfer of bone minerals from bone to serum and from serum to bone; control of citric-acid content of serum, intestinal wall, bone, and other

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organs; preparation of bone matrix for calcification, and control of renal tubular reabsorption of amino-acids.

Secondary functions: Calcification of bone matrix (*via* increased serum-calcium level); control of renal excretion of phosphate (dependent on the functional state of the parathyroid glands), and control of the serum level of alkaline phosphatase (*via* its action on osteoblasts and probably on osteoclasts and chondroblasts).

The most important effect is on the intestinal absorption of calcium and therefore also of phosphate. A second effect is the stimulation of the transfer of calcium and phosphate from the bones into the serum if the intestinal absorption is insufficient, and *vice versa* if sufficient calcium is available. The effect of vitamin D on the kidneys is negligible except in rickets (Harrison), where the tubular reabsorption of phosphate increases.

DISEASES WITH A TENDENCY TO HYPOCALCAEMIA

In vitamin D deficiency the normal serum-calcium level is maintained by hyperfunction of the parathyroids. But only in rare instances can signs of fibro-osteoclasia be observed. In a 7-year-old idiot suffering from severe vitamin-D deficiency for a long time we found not only the symptoms of rickets but also those of secondary hyperparathyroidism, i.e. subperiosteal bone resorption, disappearance of the lamina dura of the teeth at the gum margins, and alterations of the bone marrow with extensive replacement of the haematopoietic system by fibrous tissue with only a few blood cells but with numerous osteoblasts (47%) and osteoclasts (3%) remaining. After treatment with dihydrotachysterol all symptoms of rickets and of secondary hyperparathyroidism disappeared.

Amino-aciduria in rickets has been wellknown since the publications of Jonxis. In addition to this renal defect we have observed other signs of tubular dysfunction. In an 11-months-old child we saw not only amino-aciduria but also hypercalciuria in spite of a serum-calcium level of only 8·8 mg. per 100 ml. In our opinion, the hypercalciuria was probably caused by another tubular dysfunction leading to hyperchloraemic acidosis. Serum chlorides were high (113 mEq./l.), and the bicarbonate low (15·9 mEq./l.). After a total of 45 mg. of vitamin D, given in 3 doses within 6 weeks, all symptoms of rickets and of tubular dysfunction disappeared.

The cause of primary vitamin-D-resistant rickets is not a vitamin-D deficiency but a resistance to vitamin D. The most typical and most constant finding is hypophosphataemia. Fanconi and Girardet therefore proposed the name 'chronic phosphate diabetes'. The treatment of phosphate diabetes, as in chronic hypoparathyroidism, is to give high doses of vitamin D. We suggest a daily dose of 1·25 - 2·5 mg. of vitamin D corresponding to 50,000 - 100,000 i.u. The Sulkowitch test should always be strongly positive. It is advisable, therefore, to check the serum calcium at regular intervals in order to avoid hypercalcaemia.

This danger arises especially when immobilization is necessary. We saw a child suffering from typical phosphate diabetes in which immobilization after osteotomy was soon followed by a hypercalcaemic syndrome. Even under these circumstances the serum phosphate level remained very low. The main disturbance seems to be located in the renal tubules as is shown by the high phosphate clearance. The simultaneously-existing hypocalciuria could be caused either by a renal defect or by the decreased intestinal calcium absorption which is always present in phosphate diabetes.

This disease follows the dominant X chromosomal pattern of hereditary transmission, as was recently shown by Winters. In the X chromosomal dominant hereditary transmission all daughters of a sick father must be affected whereas his sons are expected to be healthy. In the case of an affected mother half of her sons and half of her daughters will present this disease. All our family trees are indeed of this type (Prader). In following them up the interesting discovery was made that several individuals had hypophosphataemia as well as a high phosphate clearance, though they presented no bone deformities.

TABLE I. FORMS OF RENAL RICKETS, SECONDARY TO DISTURBANCE OF PARTIAL FUNCTIONS

	Proximal tubule				*Distal tubule*	
Disease	*Glomerulus*	*acidogenesis*	*amino-acids*	*dextrose*	*acidogenesis*	*NH_3— production*
Glomerular hyperphosphataemic rickets	+	n	n	n	n	n
de Toni-Fanconi-Debré syndrome with and without cystinosis	n later +	+	+	+	+	?
Phosphate diabetes	n	+	n	n	n	n
Lightwood-Albright tubular acidosis with and without nephrocalcinosis	n later also +	?	n	n	+	n or +

n = normal, + = disturbed

Another form of renal rickets (Table I) is seen in the so-called de Toni-Fanconi-Debré syndrome; besides phosphate diabetes we found an amino-aciduria, a glycosuria and frequently also an anacidogenesis.

In the renal tubular hyperchloraemic acidosis, especially in the chronic form (Albright), calcium is eliminated in increased quantities into the urine to neutralize the acid metabolites. Sodium and potassium are not available in sufficient amounts because their storage in the body is limited whereas calcium can be released from the bones. The consequence is a nephrocalcinosis and/or a nephrolithiasis, and an osteoporosis and rickets.

Recently we saw a case of rickets of hitherto unknown aetiology. Even though the X-rays and laboratory findings were thought to be typical, the history failed to reveal any known cause for the development of rickets. On admission, however, a reparative giant-cell granuloma of a rib was discovered. After its surgical removal complete recovery from rickets took place within a few weeks, without any vitamin-D treatment. Obviously there was a pathogenic relation between rickets and the tumour. We believe that the tumour produced a substance which caused rickets. Two hypotheses are proposed for its possible action:

1. The substance has a vitamin-D inactivating effect.
2. It is a parathormone-like substance with selective effect on tubular phosphate reabsorption.

A hypocalcaemia of about 6 mg. per 100 ml. combined with a hyperphosphataemia of 10 mg. per 100 ml. and

more are the typical findings of chronic hypoparathyroidism. The serum chemistry can be brought to normal levels, and the other symptoms, for instance epileptiform fits, can be improved, by the administration of high doses of vitamin D (1·25 mg. daily). The danger of hypercalcaemia arising from this treatment is the same as in chronic phosphate diabetes.

DISEASES WITH HYPERCALCAEMIA

The importance of hypercalcaemic intoxication in infancy and childhood has been known only for about a decade. There are several more or less clear-cut syndromes in which the hypercalcaemic intoxication prevails. These are as follows:

1. Those of known aetiology: Primary hyperparathyroidism; overdosage of vitamin D or dihydrotachysterol; lack of cortisone in Addison's disease and after adrenalectomy; increased bone catabolism (bone tumours and leukaemia); decreased bone anabolism (immobilization); sarcoidosis; milk-alkali syndrome; and hyperthyroidism(?).

2. Those of unknown aetiology: Tumours without bone involvement, and idiopathic hypercalcaemia.

Primary hyperparathyroidism is extremely rare in childhood. Secondary hyperparathyroidism is much more frequent; in these cases overproduction of parathormone is just sufficient to maintain the serum calcium at a normal level, so that no hypercalcaemic symptoms occur.

We followed a case of severe hypercalcaemic intoxication in a 13-year-old boy with Addison's disease. All symptoms disappeared when the boy was treated with prednisone. We saw a hypercalcaemia of 15·5 mg. per 100 ml. in a case of acute lymphatic leukaemia with severe bone destruction. Cortisone stopped the proliferative leukaemic process and possibly also the absorption of calcium from the intestine. In a few days the serum-calcium level was back to normal.

In severe cases of tetraplegia in poliomyelitis, hypercalcaemia is a frequent complication. It is caused by decreased bone anabolism following immobilization. A 15-year-old girl showed nephrocalcinosis of the tips of the renal pyramids during the period of maximal renal excretion of calcium. This was apparently reversible, but some months later a nephrolithiasis occurred in spite of a completely calcium-free diet.

In the case of sarcoidosis (Besnier-Boeck disease) starting from a chronic post-traumatic ulceration on the right wrist, and treated with high doses of vitamin D, all the symptoms of a severe hypercalcaemic intoxication appeared. Treatment with prednisone stopped all hypercalcaemic symptoms quickly and improved the signs of sarcoidosis. Without prednisone the serum-calcium level remained in the range of 11 - 12 mg. per 100 ml., but anorexia, apathy, constipation, polyuria and other hypercalcaemic symptoms reappeared. The Sulkowitch reaction in the urine became strongly positive, although no vitamin D was given and the diet was poor in calcium. This case demonstrates that symptoms of hypercalcaemic intoxication may be present even with a normal or only slightly increased calcium level.

In paediatrics the most frequent form of symptomatic hypercalcaemia is vitamin-D intoxication. We have had the opportunity of observing 23 cases in the last decade. The therapy consists of the withdrawal of all drugs containing vitamin D and reduction of calcium intake (decalcified cows' milk after the method of Dent). Prednisone, which in many respects is an antagonist of vitamin D, is necessary in severe cases only.

Since our first description (1952), in collaboration with Schlesinger, Butler, Black and Girardet, of severe chronic idiopathic hypercalcaemia, a similar case was observed in Zurich. The diagnosis was established at the age of 6 months. The first symptoms of the disease appeared at the age of 2 months. The child presented all the main features (Fig. 1) of the disease with the exception of craniostenosis; the mental retardation was not severe.

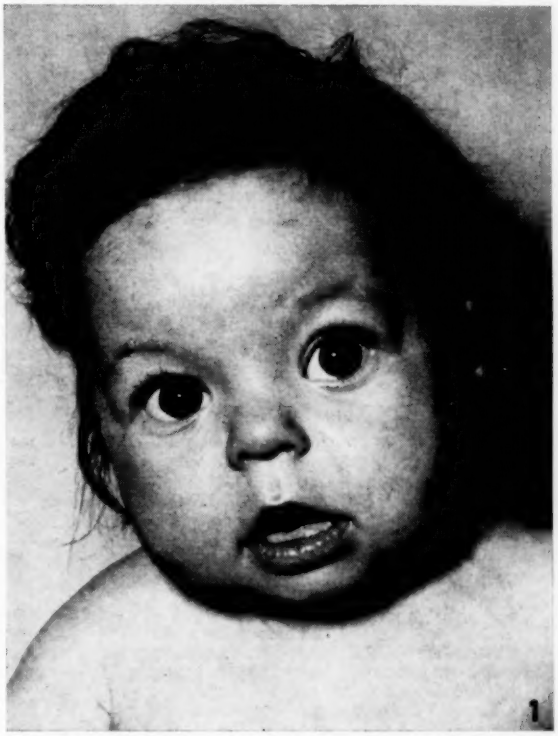

Fig. 1. Idiopathic hypercalcaemia. Typical face with hypertelorism, long upper lip, receding mandible, low-set ears, and ill-tempered appearance.

Transient improvement was achieved with prednisone as well as with decalcified cows' milk, but the child finally died at the age of 14 months in a state of hyperpyrexia. Postmortem examination showed severe nephrocalcinosis and osteosclerosis.

The usual symptoms and signs of hypercalcaemia are: anorexia, apathy, vomiting, constipation, loss of weight, polyuria, polydipsia, dehydration, osteosclerosis of metaphyses, and soft-tissue calcification.

In the serum, calcium is increased, phosphorus is variable, alkaline phosphatase is decreased, non-protein-nitrogen is increased, and cholesterol is increased.

In the urine, Sulkowitch's test is positive (+++), and

there is albuminuria, pyuria, cylindruria, and hypo- or isosthenuria.

Lightwood (1952) described the transient mild form of idiopathic hypercalcaemia. We saw only 4 cases of this disease in our hospital, while in England the incidence of this disease seems to be much higher. This fact could be explained by the difference in vitamin-D prophylaxis. In England rather high doses of vitamin D are given, usually as an addition to cows' milk or to baby foods. In our country vitamin D is seldom added to any kind of food.

The familial incidence of idiopathic hypercalcaemia became evident with the following observation. Binovular twins failed to thrive and presented all the typical symptoms and laboratory findings of the mild form of idiopathic hypercalcaemia. An investigation of the family revealed a high serum-calcium level in a 5-year-old sister not showing any other pathological signs. Both children responded well to decalcified cows' milk. One of them had to be hospitalized for a second time because of a relapse, although no vitamin D had been given. The twins continued to show a tendency to hypercalcaemia and hypercalciuria. This observation can be regarded neither as a mild nor as a severe form of idiopathic hypercalcaemia; it might be classified as an intermediate form.

A practitioner prescribing vitamin D must know whether he is facing a hypo- or hypersensitivity to vitamin D. He will think of a reduced sensitivity to vitamin D in cases with a familial disposition to rickets, with familial aminoaciduria and with accelerated growth, as for instance in premature infants.

He will have to watch for an increased sensitivity to vitamin D in cases of retarded growth, especially in endocrine disorders. Among our four cases of this group there was one child suffering from hypothyroidism and a second one presenting as a Turner's syndrome. Retarded growth with increased density of metaphyseal margins should make one cautious in using vitamin D. Children showing a premature closure of the fontanelles and the cranial sutures are also predisposed to hypersensitivity. Immobilization of a normal child may lead to symptoms of hypersensitivity if a normal dose of vitamin D is administered. We observed this in a 4-year-old boy suffering from Perthe's disease.

It is evident from this short review that some children require extremely large doses of vitamin D while others show a severe hypercalcaemia without ever having received any vitamin D. In our opinion the various intermediate syndromes represent a gradual transition between the two extremes of hypo- and hypersensitivity to vitamin D.

SUMMARY

The normal physiology of calcium and phosphorus is discussed. The various factors responsible for the control of serum calcium within narrow limits are evaluated.

Diseases with a tendency to hypocalcaemia and those with a tendency to hypercalcaemia are discussed and differentiated.

QUESTIONS ANSWERED : VRAE BEANTWOORD

THREADWORMS

Q—*The piperazine group of anthelminthic drugs is often recommended in pharmaceutical literature for the treatment of threadworms. Are these drugs really satisfactory? What regime should one employ for the eradication of this common and troublesome infection?*

A—

'Not half so big as a round little worm
Prick'd from the lazy finger of a maid;'
Romeo and Juliet, I, iv, 53.

The problem of man and his parasites is as old as man himself, and in the main they live peaceably together. Threadworms are no exception, and the number of patients who have symptoms from their infection is far exceeded by those who are infected but well.

Since threadworms are ubiquitous and man the only necessary host, the ova lie in the fomites and fingers of an affected family, and reinfection easily occurs after successful treatment of the patient.

Piperazine is an excellent vermifuge for threadworms and in adequate doses effects a cure in practically 100% of cases. It should be given in a dose of 50 - 75 mg. per kg. of body-weight per day for 7 days, and a second course should be given after a week's rest. An elixir of piperazine citrate containing 500 mg. per teaspoon (4 ml.) is the most convenient method of administration and the day's requirements may be given in a single dose. As a rough guide the dose is 1 teaspoonful per year of age per day (e.g. for a three-year-old child 3 teaspoonsful daily) in the courses prescribed above. The maximum daily dose is 1 fl. oz. (4·0 g. of piperazine hydrate).

But this is not enough. All the children must be treated at the same time, and the mother or other people who regularly handle the infected child must also receive piperazine in adequate dosage. Without this the infection will certainly recur, and the mother will continue to peer anxiously at the stools of the luckless offspring.

It is unnecessary to restrict the diet or to apply ointments to the anus. Over-zealous attempts to prevent children from scratching around the anus will not help particularly in eradicating the worms.

However, attention must be paid to other conditions which may lower the resistance of the colon to parasitic or chronic infection. Each must be treated on its merits after the eradication of threadworms, which may be assumed to be complete after a full course of piperazine.

The cost of treating a family of, say, mother and 3 children should not exceed £1 10s. 0d. if the piperazine preparations are bought in 40-oz. containers.

BOOKS RECEIVED : BOEKE ONTVANG

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South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL : VAN DIE REDAKSIE

PAEDIATRIC VIEWPOINT

What exactly is paediatrics? Why is it spelled that way? Is it a separate 'discipline' to be taken seriously or just the result of a pressure-group serving its own ends? Is the slightly derogatory term of reference 'kids', used by students and nurses, a reflection of widely-held opinion? Or is paediatrics something worse, to be suppressed as much as possible, since it threatens to claim a place in the front rank of medicine and endanger the already diminishing status and shakily-entrenched privilege of hierarchies of physicians, surgeons, and obstetricians? If it is important, what are the medical schools, nurses' training centres, and public health authorities doing about it? And what do paediatricians discuss at their congresses — exercises in the occult or elaborate techniques for the changing of diapers? Why produce a paediatric number of the *Journal*?

These questions are provoked by the attitudes of those people, lay and medical, with whom paediatricians are in daily contact. There is a feeling of suspicion about the whole business, of paediatrics becoming an *enfant terrible* in this country. It clamours for more teaching time, more beds, more nursing and auxiliary services, for special hospital facilities, for convalescent homes, and of course for more money for its activities and research. And it is not the only one of medicine's 'problem children'. There are others growing up and, sooner or later, they also will have to be admitted to the limelight from their present semi-obscurity in the wings. The processes of evolution are not confined to zoology, and paediatrics in South Africa has a long way to go. In many other respects, notably virology, nutrition, and cardiac surgery, this country's experts are of international status and are accorded approval at home. Much of their work has been done in the treatment of children, but the basic requirements of paediatrics continue to be largely ignored.

Dorland's *Illustrated Medical Dictionary* defines paediatrics (or rather, American fashion, 'pediatrics') as 'that branch of medicine which treats of the child and its development and care and of the diseases of children and their treatment'. The word is derived from the Greek *pais, paidos*, a child, and the American way of spelling it has probably led to the confusion in some people's minds that paediatrics deals with diseases of the foot (from the Latin, *pes, pedis*, a foot). But the confusion does not end there, since the general vague mental picture of a paediatrician is that he is merely a 'baby doctor' and the inference is that he should be treated as such, the baby being parsed as an adjective and not as a noun. The care of children is the common lot of a very large proportion of the human race at some time in their lives, but their equipment for the job is negligible. This applies to medical and nursing personnel almost as much as to the layman. There is vast and urgent need for expert paediatric knowledge and guidance in every type of medical institution, except those for alcoholics, and there is no discernible recognition of this at present. The lay public is still in paediatric Standard I.

Approximately a third of any general practice is paediatric work in terms of the definition above and it is not many years since the statement was made that 'I'd as soon see the devil himself come into my consulting room as a young child'. The era of castor oil as a panacea for all ills in childhood has not yet passed and the prophylaxis of disease in childhood is an unopened book for large sections of our population of all races. The special requirements, meticulous attention to hygiene, detailed care and observation, psychological needs of sick children, and what the Americans call T.L.C. (tender loving care) in every aspect of the work, are fundamental. But they have yet to make the faintest impression, let alone any sort of impact, on the vast majority of those who hold the children's future in their hands. And, though it is almost incredible, this applies to women even more than to men. In other civilized countries paediatrics has been an established branch of medicine for at least forty years and much of the earliest work leading to modern medical practices was first done in the treatment of children by paediatricians or their immediate associates. Fluid replacement and biochemical investigations were widely used in paediatric circles long before they were applied to adults, and the work of Hartmann, Gamble and Darrow, and others was done in children. But in South Africa, in 1960, there are only two professors concerned with paediatrics, a few more lecturers in charge of university departments, a mere handful of paediatric-trained nurses and no sign of any disposition to increase this miserably token force.

Far too many of our children, in and out of the hospitals, are cared for according to the tenets of their own or someone else's grandmother. Medical students and postgraduates, these days, have a modicum of instruction in paediatrics. As interns, they will be helped by nursing staff, if they have trained nurses to care for their patients, who will largely follow the diets and practices of their mothers, who were instructed in the art by *their* mothers, half of whose children died before the age of five years. The less fortunate doctors, and their paediatric patients, will be at the mercy of individuals trained, or in the process of being trained, by instructresses who are themselves untrained in paediatric nursing. Or, and this is not unknown, the attendants will be untrained and often untrainable. Folk-lore has been tried over centuries, with deplorable results. Surgeons do not have to work with untrained staffs in pre-Listerian conditions. Physicians treating adults achieve their effects by drugs and the cooperation of the patient. Obstetricians, to some degree, are at the mercy of their staff and surroundings for the safety of their adult patients, and in exactly the same position as paediatricians otherwise. In other words, the needs of one branch of the profession are much the same as those of the others. But when the patients cannot, because of age or illness

or merely from timidity, voice their needs and complaints, the deficiencies in our ritual become glaringly obvious. In paediatrics they became so long ago, and it was realized that the maintenance and the restoration of health in children, still more in infants and in the newborn, demanded far more particular knowledge and attention to detail than was needed in other fields of medicine. This applies to dietetics, hygiene, environment, and even to clothing.

Diseases of children differ in some degree from those of their elders partly because of the size factor and partly because of the greater incidence of non-degenerative types of illness. The outlook of the paediatrician is towards either the maintenance or the complete restoration of health, as opposed to the preservation of what health remains in most adult patients, or the repair of some form of damage as in most of surgery. To that extent paediatrics is a different but not an alien discipline. It recognizes the need to cooperate with many other divisions of medicine to achieve its aims but it is not a 'very small subject' capable of being absorbed by any other. The highest standard of paediatrics is possibly Utopian. The current general standard, in all kinds of ways, could and must be improved. Until it is, it is to be hoped that paediatricians will continue to be agitators.

The present number of the *Journal* should serve to show that the professional interests of paediatricians are in line with what has been indicated above. The discussions at the recent paediatric congress have a bearing on many medical problems, though here their background is the paediatric age group.

RENALE HIPOFOSFATEMIE

Sedert die publikasie van Richard Bright se referaat in 1827 was dit gebruiklik om die term chroniese renale ontoereikendheid te assosieer met die kliniese en patologiese bevindings soos deur hom beskryf. Die patogenese van die stikstofretensie, albuminurie, metaboliese asidose, en anemie is nog nie in elke opsig verduidelik nie, maar daar is algemene ooreenstemming dat ons hier te doen het met versaking van die nierfunksie in sy geheel. Daar is 'n vermindering van die aantal funksionerende nefrone met 'n ooreenstemmende daling van die filtrasie deur die glomeruli asook verstoring van die tubulêre funksies, soos gevind by gevalle van chroniese glomerulonefritis, arteriolêre nefrosklerose, en chroniese piëlonefritis.

Gedurende die laaste paar dekades het 'n toenemende aantal navorsers intensiewe aandag gewy aan 'n groot verskeidenheid van renale verstorings wat in teenstelling staan met die sg. Bright se siekte.[1,2,3] Hierdie toestande is in die eerste instansie gekenmerk deur tekens van renale ontoereikendheid veroorsaak deur defekte van die tubulêre funksies. Albuminurie en stikstofretensie is gewoonlik afwesig, hoewel glomerulêre ontoereikendheid uiteindelik mag ontwikkel. Die teenswoordige belangstelling in die laasgenoemde groep van siektetoestande kan toegeskryf word aan verskeie faktore, byvoorbeeld die feit dat die toestande behandelbaar en die skade gewoonlik omkeerbaar is, in teenstelling met chroniese nefritis. Die sindrome bied ook 'n unieke geleentheid aan om renale meganismes en geneties-bepaalde siektetoestande te bestudeer. Baie van die sindrome gaan gepaard met aminosurie, en die onlangse ontwikkeling van chromotografiese en ander tegnieke om aminosure wat in die urine afgeskei word te bepaal,[4] het as 'n verdere stimulus gedien om belangstelling te bevorder.

Die patogenese van die siektetoestande wat veroorsaak word deur gebrekkige funksie van die renale konkelbuisies berus op defektiewe herabsorpsie van stowwe in die glomerulêre filtraat. Byvoorbeeld, defektiewe herabsorpsie van (a) water gee aanleiding tot nefrogeniese diabetes insipidus,[5] (b) glukose → renale glukosurie, (c) fosfate → renale hipofosfatemie (d) glukose, fosfate, en aminosure → Fanconi se sindroom, en (e) alkalië → renale asidose. So is daar nog etlike ander defekte en aangesien amper enige *kombinasie* van defekte oënskynlik kan plaasvind, sowel as *enkele* defekte, kry ons 'n groot aantal verskillende interessante siektetoestande, die meeste waarvan selde voorkom. Renale hipofosfatemie is een van die algemeenste.

Die terminologie van hierdie siektes is menigvuldig en taamlik verwarrend. Fanconi se naam word soms losweg gebruik om 'n hele paar sindrome in die groep te bestempel. Dit behoort beperk te word tot (d) hierbo. De Toni en Debré se name behoort na regte bygevoeg te word aangesien hulle ook oorspronklik dergelike gevalle gerapporteer het. Eintlik sou dit verkieslik en minder verwarrend wees om name te vermy soos verskillende mense, o.a. Fanconi self, alreeds aangedui het.

Wat renale hipofosfatemie betref, word 'n dosyn of meer terme gevind in die literatuur om dieselfde siektetoestand aan te dui. Die benaming vitamien D-weerstandige rachitis[6,7] is die populêrste. Daar is egter ander tipes van rachitis wat vitamien D weerstandig is. Die toestand is nie ‚weerstandig' as massiewe dosisse van die vitamien toegedien word nie, en daar is geen weerstandigheid teen die vergiftingseffekte nie. Die term is dus nie baie aanneemlik nie.

Al die bevindings by hierdie gevalle kan verduidelik word op grond van defektiewe funksie van die proksimale renale konkelbuisies. Oënskynlik is daar 'n defek van die ensiemsisteem wat die transport van fosfate beheer. Die tubulêre defek is gewoonlik, indien nie altyd nie, kongenitaal. Die swaannek-deformiteit van die proksimale tubulêre stelsel[8] wat gevind is by verskeie gevalle van verwante renale verstorings, is oënskynlik nie die patologiese letsel wat in verband staan met renale hipofosfatemie nie.

Ander faktore wat 'n rol speel by die patogenese van hierdie siekte moet oorweeg word. Albright[9] het gemeen dat hiperparatiroïdisme 'n hoofrol speel en het dan ook hiperplasie van die paratiroïedklier aangetoon. Hierdie hipotese verklaar egter nie al die feite nie. Die effek van vitamien D op die funksionele bevoegdheid van die proksimale konkelbuisies het die laaste tyd baie aandag geniet. Fanconi stel renale hipofosfatemie of weerstandige rachitis aan die een uiterste van 'n spektrum van siektetoestande wat gekenmerk word deur verskillende grade van gevoeligheid vir vitamien D. By renale hipofosfatemie sal daar

dan die laagste graad van gevoeligheid wees teenoor vitamien D. Chroniese hiperkalsemie van suigelinge kom aan die ander end van die spektrum, en word beskou as 'n toestand wat veroorsaak word deur oorgevoeligheid vir hierdie vitamien.

Die skelet self se aandeel in die patogenese is oënskynlik heeltemal passief. Verwyderde beenweefsels van pasiënte sal kalsifiseer in die teenwoordigheid van kalsium en fosfor. Die bene kalsifeer nie as hul geïnkubeer word met die ongewysigde serum van onbehandelde pasiënte nie.

Die siekte is oorerflik op 'n dominante seksverbonde genetiese basis. Winters en sy medewerkers,[10] byvoorbeeld, het 'n familie bestudeer na hul die siekte by 'n kind ontdek het. Daar was 283 lewende familielede, waarvan driekwart ondersoek is. Daar was rachitiese deformiteite teenwoordig by 25 en hipofosfatemie by 11 sonder deformiteite. Kliniese ondersoeke sonder meer is dus nie voldoende nie. Hulle het gevind dat daar geen geval van die siekte voorgekom het waar die ouers altwee normofosfatemies was nie. Egte sporadiese gevalle word egter af en toe gerapporteer.[11]

Al die kliniese verskynsels kom voor in die skelet. Deformiteite word gewoonlik bespeurbaar as die kind begin te loop. Die kenmerkende tekens van rachitis is teenwoordig en röntgenografiese ondersoeke toon ook die tipiese rachitiese verskynsels. Die pasiënt verkeer andersins in blakende gesondheid en het 'n normale lewensverwagting, in teenstelling met dié tipe van renale rachitis wat veroorsaak word deur chroniese nierversaking. Op grond van bogenoemde bevindings word die kind, redelik genoeg, behandel as 'n geval van rachitis met die gewone terapeutiese dosis van vitamien D. Ongelukkig het daar in die verlede gewoonlik 'n tydperk van gemiddeld twee jaar verloop voor die geneesheer bewus geword het van die weerstandige aard van die siekte, en gedurende hierdie tyd ontwikkel uitgesproke deformiteite en dwergisme.

Behandeling met massiewe dosisse van vitamien D, soms soveel as een miljoen eenhede per dag, of 25 mg. calciferol, is van beproefde waarde, maar die geneesheer moet onthou dat sulke dosisse giftig mag wees en die aanbevole voorsorg moet noukeurig nagekom word.[2] Die behandeling gaan 'n onbepaalde aantal jare lank voort. Na puberteit sal dit waarskynlik moontlik wees om die dosis te verminder.

Baie gevalle is in die verlede oor die hoof gesien en medici moet op hul hoede wees om die siekte vroeër te diagnoseer en om te onderskei tussen gewone rachitis weens eksogene oorsake, renale rachitis wat voorkom by gevalle van chroniese nefritis met hiperfosfatemie, en die tipes van renale rachitis wat veroorsaak word deur verstoring van die tubulêre funksies.[2]

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PAEDIATRIC SURGERY

That well-known story in which the elderly practitioner inquires of the fledgling otorhinolaryngologist which nostril he is going to specialize in, emphasizes the often ridiculously high value placed nowadays on specialization. But in this latter half of the twentieth century, with rapid advances being made almost daily in all branches of science, including medicine, it is becoming increasingly apparent that the specialist is here to stay. Almost every organ in the adult now has its expert, whereas the child, especially the surgically-ill child, for too many years has had deaf ears turned to its insistent cry. It is interesting indeed that paediatric surgery, which only in the last few decades joined the family of specialties, has now grown into a lusty 'infant', howling for recognition and demanding a place at the table.

There are many reasons for the earlier cruel neglect of paediatric surgery; e.g., the patient is inarticulate, there is a widespread misconception that children can be treated simply as miniature adults, and the fact that the salvage rate of congenitally-deformed infants has been low. In addition the financial position of the little patient is often precarious because his young parents are on the threshold of their married partnership and usually in no position to afford the fees of a specialist.

There is little to compare with the satisfaction obtained in remedying an otherwise fatal neonatal anomaly and then seeing the infant thrive and watching, with the happy parents, the child growing up. Where in surgery can one expect a sixty to seventy year prognosis, other than in the surgery of infancy?

A demand has been created for experienced surgeons who will be prepared to devote all their time to paediatric surgery. This demand is now being met. All over the world more and more men are training to become proficient in this branch of surgery — an exacting branch, requiring specialized knowledge of the anatomical, physiological, metabolic, and psychological needs of children, and demanding the utmost gentleness, skill, and precision in operative work. The knowledge and the skill can only be acquired by constant daily contact with small children, close personal pre- and postoperative supervision, and frequent experience in operating on small infants. Training of this nature is long, and the aspirant paediatric surgeon must have a great love of children, from which will surely stem a deep desire to obtain and give his best for the child who is in need of surgical care.

The training of specialists in paediatric surgery can only be accomplished in a children's hospital, where, under the guidance of a senior surgeon (whose primary, if not total, interest is children's surgery) the proper practice of the subject can be taught. In such a hospital, which must be fully staffed and adequately equipped, the apprenticeship will be a long one. It should follow a period of training in general surgery, including the major subdivisions of orthopaedics, plastic surgery, urology, and thoracic and cardiac surgery. For the paediatric surgeon is a modern example of that almost archaic species, the general surgeon. His interests range from clubfeet to naevi; from undescended testes to holes in the heart; from oesophageal atresia to enuresis.

In South Africa, too, paediatric surgery is growing up, thanks largely to the interest accorded it during the last ten years in Cape Town. At the Red Cross War Memorial Children's Hospital in Cape Town the high standard of paediatric surgery compares favourably with that of similar centres in the United Kingdom, the United States, Switzerland and Denmark — indeed anywhere in the world. There is a full-time consultant surgeon, unique in South Africa, whose time is devoted entirely to paediatric surgery, and there are registrars who maintain a night and day watch on all major neonatal surgical cases. No mention of paediatric surgery in South Africa would be complete without coupling it with the name of Prof. J. H. Louw of the University of Cape Town, who has always strenuously exerted himself in the cause of this demanding specialty.*

It is only by whole-hearted and full-time attention that unnecessary loss of life can be prevented, and the best results obtained. The day of the casual paediatric surgeon, operating on infants, perhaps once a year, knowing no more about their special care than about the metabolism of magnesium, is fortunately fading. With the widespread, ever-increasing awareness of the importance of paediatric surgery, the consequences cannot but be beneficial to thousands of tiny patients to whom our duty is crystal-clear — to preserve that most precious thing in the world, life itself.

* A paper on 'Surgery in the newborn' by Prof. J. H. Louw, which was presented at the Fourth Congress of the South African Paediatric Association (M.A.S.A.), Cape Town, 5 April 1960, was published in the issues of the *Journal* for 13 and 20 August 1960 (**34**, 686 and 707).

STUDIES IN RICKETS IN THE CAPE PENINSULA

I. CRANIAL SOFTENING IN A COLOURED* POPULATION AND ITS RELATIONSHIP TO THE RADIOLOGICAL AND BIOCHEMICAL CHANGES OF RICKETS

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Rickets still occurs frequently in tropical and sub-tropical countries. There have been recent reports from Israel,[1] the Phillipines,[2] Nigeria,[3] Singapore,[4] and South Africa.[5,6] Feldman in 1950 noticed that rickets was common in Johannesburg, although he did not assess its incidence. He thought that the urbanized Native infant was not sufficiently exposed to sunlight.[6] On the other hand, Kark and le Riche, in a survey of Native school children, found it to be uncommon in the rural areas.[7]

In any survey of rickets the diagnosis of the early case presents a problem. Histological abnormality at the costo-chondral junction is probably the earliest sign of rickets, but without this evidence cases must be assessed by clinical, radiological, and biochemical changes.

Radiological changes probably occur only when rickets is fairly advanced. Craniotabes is sometimes cited as the earliest clinical sign of rickets,[8,9] but below the age of 3 months this phenomenon can occur in normal children.[10] Even over this age, some authorities have regarded it as a normal physiological variant.[11]

Routine biochemical tests in the investigation of rickets include serum levels of alkaline phosphatase, inorganic phosphorus, and calcium. Abnormal phosphatase levels have been found to be a reliable index of early activity, preceding radiological changes, and more constant than reduced serum inorganic phosphorus.[13,14]

Objects of this Investigation

1. To determine the incidence of rickets in a hospital population of urbanized Coloured out-patients.

2. To assess the frequency and significance of craniotabes between the ages of 3 months and 1 year.

3. To investigate the value of altered serum levels of alkaline phosphatase, phosphorus, and calcium in diagnosing early rickets and in assessing progress.

* Coloured signifies people originating from 4 principal stocks: Hottentot, Bushman, European and, more recently, Bantu. Ten of these subjects were pure Bantu.

METHODS

All children between the ages of 3 months and 1 year attending at Paediatric Out-patient Department at Groote Schuur Hospital during the month of October 1959 (105 in all) were examined for clinical signs of rickets. Special attention was directed to the presence of cranial softening and its severity as detected by palpation. Cranial softening was not considered to be present unless it involved an area about 1 inch in diameter. It was graded as mild when only a small area of the occipital bone was involved — occasionally unilaterally. If the softening was more extensive and indented with only slight pressure, it was classified as severe.

Children aged 3 - 12 months (selected at random) with cranial softening, who were found during the months of September and October, were further investigated for other evidence of rickets. Radiographs of the wrist were obtained in all these cases and, in many, chest films. The X-ray films were examined by at least 4 observers (3 of whom saw all the films†) and were classified as showing advanced rickets, early rickets, or no rickets. There were some cases in which it was difficult to be certain if rickets was present in its earliest stage, and these were appropriately classified as 'dubious'. A control group of Coloured children between 3 and 12 months of age, without cranial softening, were also X-rayed to assess the incidence of rickets. Serum-alkaline phosphatase, inorganic phosphorus, and calcium levels were determined. Most patients were seen again 4 - 8 weeks later when radiographs and biochemical tests were repeated. Of 23 children who had rickets and were seen subsequently, 8 received calciferol (ostelin forte,‡ 1 c.c. intramuscularly, i.e. 600,000 units of vitamin D_2) and the remainder were not treated.

† Dr. L. Werbeloff and the authors of this article.

‡ Supplied by Messrs. Glaxo-Allenburys (S.A.) (Pty.) Ltd.

RESULTS

1. *Total Incidence of Cranial Softening Seen During One Month*

A total of 105 patients between 3 months and 1 year of age were reviewed (Fig. 1), 49 of whom had cranial softening. They were divided into 2 groups according to age — children of 3 - 6 months, inclusive, in group 1, and 7 - 12 months in group 2. The incidence of cranial softening was higher in group 1 (75%) compared to group 2 (27%). There was also a higher incidence of severe cranial softening in the younger age group (25%, compared to 4% in group 2).

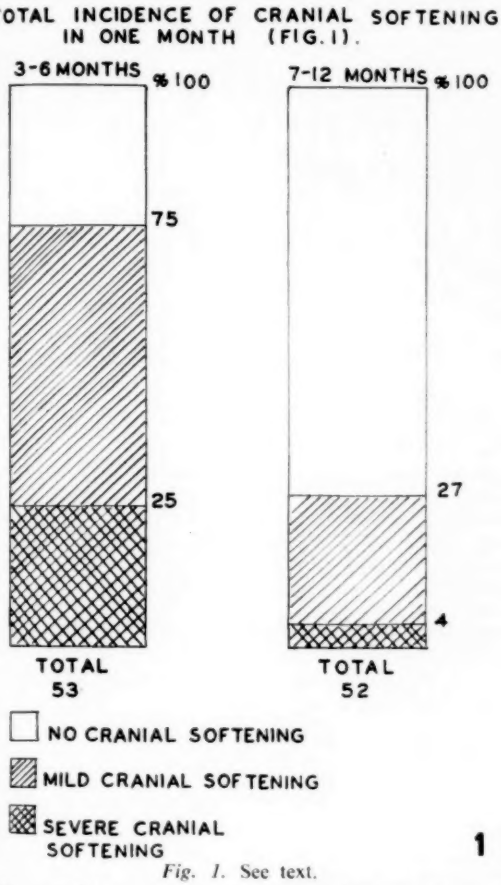

Fig. 1. See text.

2. *Significance of Cranial Softening*

In group 1 over 40% of cases with cranial softening (14 out of 34) had definite radiological evidence of rickets. In group 2 the incidence of rickets in cases with cranial softening was higher (over 60% — 13 out of 21). This difference is not statistically significant (P ·1). Cases with severe cranial softening were no more liable to rickets than those with mild cranial softening (Table I).

In a control group of subjects without cranial softening, 13 were between 3 - 6 months of age, and 14 between 7 - 12 months. None of the younger group had rickets, but 5 of the older group had radiological rickets.

TABLE I. COMPARISON OF CASES WITH SEVERE AND MILD CRANIAL SOFTENING

	Cranial softening	*No rickets*	*Radiological rickets*		*Total*
			Mild	*Severe*	
Severe	27	16	8	3	11
Mild..	28	12	7	9	16
Total	55	28	15	12	27

It is noteworthy that rickets actually appears commoner with 'mild' craniotabes than with the 'severer' grade. This is evidently related to the age incidence, since radiological rickets was commoner in the 7 - 12-month group (60% of all cases with cranial softening) than in the 3 - 6-month group (40%), while severer craniotabes was commoner at 3 - 6 months (24 cases) than at 6 - 12 months (3 cases).

BIOCHEMICAL CHANGES IN RICKETS (TABLE II)

The marked difference in mean alkaline-phosphatase levels between patients with definite rickets and those with dubious or no rickets, was significant ($P<·001$). There was no significant difference in the mean levels of those patients with dubious rickets, cranial softening with no rickets, and controls without cranial softening. The difference in the mean levels between advanced and early rickets was possibly significant ($P<·05$).

There was no difference in inorganic phosphorus levels in the patients with dubious radiological changes, controls without cranial softening, and those with cranial softening. Although the mean values fall progressively as rickets becomes more advanced, the differences between the various groups are not significant.

There was a disturbing overlap in individual cases in various groups — some patients with rickets had normal serum-alkaline phosphatase and phosphorus readings, while some without radiological abnormality had elevated levels of alkaline phosphatase.

There was no correlation between biochemical changes and the severity of cranial softening. Half the patients with radiological rickets had a serum calcium below 9 mg. per 100 ml. Two cases with early rickets had a calcium × phosphorus quotient above 40, yet neither showed any evidence of healing.

PROGRESS OF CASES

Radiological

Radiological improvement was observed (after 4 weeks) in 11 cases of rickets, 7 of whom had received calciferol and 4 not. No change was noted in 7 patients, 6 of whom had had no therapy, and the radiological appearances were worse in 5, none of whom had received treatment.

Radiological rickets did not develop in any patient with cranial softening who had normal X-ray appearances originally and who received no treatment.

In cases of originally doubtful radiological appearances definite changes developed in only 1 case. In 3 cases the changes remained doubtful, and in 4 cases, 1 of whom had received calciferol, the appearances became definitely normal.

Cranial Softening

Twenty-two cases of rickets with cranial softening were re-examined after a 4 - 8 week interval. Cranial softening was still present and had not changed in 18 of these. In some of these cases the rickets had healed radiologically. Eleven patients with cranial softening, but without

TABLE. II. BIOCHEMICAL CHANGES IN RICKETS

Controls		*Cranial softening with normal radiological appearance*		*Dubious rickets*		*Early rickets*		*Radiologically advanced rickets*	
A.P.	*I.P.*	*A.P.*	*I.P.*	*A.P.*	*I.P.*	*A.P.*	*I.P.*	*A.P.*	*I.P.*
Mean*12 (3·9)	5·8 (0·6)	18 (6·1)	5·4 (0·7)	16 (5·1)	5·8 (1·2)	27 (13·4)	4·4 (1·5)	42 (26·6)	3·8 (1·1)
21·6	6·7	26·4	4·8	27·4	7·9	47·5	7·0	106	2·7
18·3	6·0	24·6	5·4	22·3	5·0	45·0	2·8	57·5	
17·9	4·6	24·1	5·6	18·1	4·9	41·9	3·7	38·9	5·8
16·3		23·1	4·3	16·3	5·4	34·1	5·1	35·6	3·6
14·9		19·6		16·2		30·2	6·7	35·0	4·5
13·5	6·8	19·0	5·4	15·1	7·8	22·8	3·0	28·1	4·2
12·5	5·9	18·4	4·8	12·7	4·5	22·8		24·3	2·9
12·1	1	17·2	5·2	12·0		21·6	3·8	15·8	2·3
11·7		16·4	4·7	11·7	4·6	16·5	3·1		4·4
11·0	5·7	15·9		8·5	6·1	10·3			
10·0	6·6	15·1	4·5			4·3			
9·6		9·4	5·9						
9·3	4·2	8·1							
9·2	5·4	7·3	6·3						
8·6			6·7						
8·0	5·2		5·6						
7·0			6·5						
	5·5								
	6·8								
	5·7								
	5·5								

A.P. = Serum alkaline phosphatase levels (Sinowara-Bodansky units).
I.P. = Serum inorganic phosphorus levels (mg./100 ml.).
* Standard deviation in brackets.

radiological rickets, were likewise re-examined. Cranial softening was not detected at the subsequent examination in 6, and had improved in 2.

Biochemical Changes (*Tables III and IV*)

(i) *Alkaline phosphatase*. Serial biochemical changes were not followed in all cases. In 4 cases showing radiological healing the alkaline phosphatase fell in 2 and rose in 2. In 2 cases in which the radiological appearances changed for the worse the alkaline phosphatase rose. In cases of biochemical rickets showing no radiological changes the alkaline phosphatase remained unchanged in 1 and improved in 1.

In cases in which there was no evidence of rickets or dubious rickets originally, and in whom the radiological picture did not change, the alkaline phosphatase became higher in 4, lower in 1, and was unaltered in 4.

Biochemical changes appeared to have no prognostic value in the interesting group where radiological signs were originally doubtful. Cases with elevated alkaline phosphatase levels progressed favourably to radiological healing, whereas the 1 case in which the radiographs became worse had a normal alkaline phosphatase reading.

(ii) *Inorganic phosphorus*. In patients with rickets who showed radiological improvement, the serum-phosphorus level rose in 2 and remained unchanged in 2.

In those cases in which the rickets progressed, the serum phosphorus was slightly depressed in 2 cases, and in those cases in which there was no change in radiological ap-

TABLE IV. BIOCHEMICAL CHANGES IN FOLLOW-UP EXAMINATIONS. (2. NO RADIOLOGICAL RICKETS*)

Alkaline phosphatase		*Phosphorus*	
1st	*2nd*	*1st*	*2nd*
22·3	32·5	6·0	5·3
18·1	28·7	6·7	6·0
15·1	22·6	7·8	6·3
19·0	29·2	5·4	6·3
15·1	14·1	5·6	7·7
15·9	10·4	4·7	6·4
7·3	12·8	4·5	5·5
8·1	7·2	5·6	6·7
24·1	16·2	5·9	6·4
		5·4	6·3
		5·0	6·2
		4·9	6·3

* No change in subsequent X-rays.

TABLE III. BIOCHEMICAL CHANGES IN FOLLOW-UP EXAMINATIONS. (1. RADIOLOGICAL RICKETS)

Improved *				*No change* *				*Worse* *			
Alkaline phosphatase (units)		*Inorganic phosphorus (mg. per 100ml.)*		*Alkaline phosphatase (units)*		*Inorganic phosphorus (mg. per 100 ml.)*		*Alkaline phosphatase (units)*		*Inorganic phosphorus (mg. per 100 ml.)*	
1st	*2nd*	*1st*	*2nd*	*1st*	*2nd*	*1st*	*2nd*	*1st*	*2nd*	*1st*	*2nd*
47·5	30	4·5	5·7	24·3	23·4	3·6	5·3	12·0	30·9	5·1	4·5
38·9	15·1	3·3	4·3	57·5	27·8	2·7	2·4	22·0	41·9	4·4	3·9
16·5	23·4	4·4	4·1								
27·0	62·0	5·8	5·5								

* On radiological examination.

pearance it became higher in 1 and was unaltered in another.

In cases showing unchanged normal or dubious radiological appearances, most had a higher phosphorus level on the second occasion (in no instance was the serum phosphorus below 4·5 mg. per 100 ml.).

DISCUSSION

1. *Incidence of Rickets*

Approximately 50% of Coloured children between the ages of 3 and 12 months had cranial softening and in this investigation half of these (i.e. 25% of the total) had definite radiological evidence of rickets. In addition there are those children in the 7 - 12-month age group who have rickets without cranial softening. This would increase the total incidence of rickets in the 3 - 12-month group to over 30%. We have excluded all cases in which the radiological diagnosis was not definite and those cases who had slightly abnormal biochemical findings but no radiographic evidence of rickets. In fact the biochemical and radiological findings were completely normal in only 10 of the 51 cases with cranial softening.

However, both pneumonia and gastro-enteritis are commonly associated with rickets and, since these are the two commonest complaints of out-patients, it is likely that we are obtaining an exaggerated estimate of the incidence of rickets in general. It is also possible that the incidence is especially high in the spring months.

Nevertheless Follis,[15] in a survey of rickets in the USA between 1925 - 1942, observed an incidence of 63% in the first 2 years of life (based on histological changes in autopsy material). Gillman[16] found an incidence of 50% in Johannesburg in children under 1 year, based on the same criteria. Histological evidence, however, cannot really be compared with that obtained by other methods. The incidence of rickets in Great Britain, where bread was enriched with calciferol, is very low. In a recent survey only 17 out of 3,328 children had active rickets.[17] It is also uncommon in New Zealand,[18] but is common in several tropical and sub-tropical parts of the world, as remarked above.

2. *Significance of Cranial Softening*

The incidence of this sign seems to vary in different geographical areas, being a very rare feature of rickets in Nigeria[3] and Singapore,[4] but common in Cape Town among both Coloured and Bantu children.

Approximately half the cases of cranial softening had no radiological evidence of rickets. It is possible that the cranial softening in these cases was either the first indication of rickets, the only remaining sign of rickets, or a normal variant. We have not observed that rickets develops in any case of craniotabes which did not originally have radiological signs, nor was there evidence of healed rickets on the normal radiographs, so that we feel it is unlikely to be either an early or a residual manifestation of rickets in these cases. We have also seen cases of rickets healing radiologically while the cranial softening persisted, and conversely, cranial softening becoming normal before radiological healing. We feel, therefore, that approximately half the cases of cranial softening bear no relationship to rickets, and may be physiological. However, the fact that the other half was associated with radiological rickets is no proof that it, too, was not physiological, unless it is shown that rickets is not found in the *absence* of craniotabes.

In the 3 - 6-month age group we were in fact unable to detect rickets in the absence of cranial softening, so that at this age it appears that some cases of cranial softening are directly associated with rickets. In the older group there were cases of rickets with no cranial softening, although the incidence of rickets in this group was less than in those with cranial softening (approximately half). There does seem to be an increased likelihood of cranial softening being associated with rickets above 6 months than below this age (but this has not been proved statistically). Furthermore, craniotabes not associated with radiological rickets appears to behave differently in follow-up examinations. In most of these cases it improved or 'healed' completely without treatment, whereas, when associated with definite rickets, it was more likely to persist unchanged.

In conclusion, there appear to be 2 varieties of cranial softening: one completely unassociated with rickets, and possibly physiological; and the other, an identical softening which is associated with rickets and which displays a different natural history.

3. *Significance of Biochemical Changes*

Although most cases of rickets had elevated serum-alkaline phosphatase and depressed phosphorus levels, there were cases in which the serum levels were not altered, so that these parameters cannot therefore be regarded as reliable indices of activity. High alkaline-phosphatase levels were not always associated with low serum phosphorus, as was observed by Wayburne and Dean.[12] There were also cases with normal radiological appearances in which the serum levels were abnormal. There was no evidence that biochemical changes in fact preceded radiological abnormalities, as there was no difference in subsequent radiological appearances in these cases.

The cases which present the most difficult diagnostic problems are those with dubious radiological appearances, and it was hoped that biochemical changes would be of assistance in these.[13, 14] However, there was no correlation between biochemical abnormality and the future course in this group of patients, most of whom recovered in spite of having abnormal serum chemistry. One case, however, progressed to definite radiological rickets with normal serum chemistry. A change of X-ray diagnosis on follow up from 'dubious' to 'normal' presumably indicates that rickets was actually present in the 'dubious' phase.

Serial serum-alkaline phosphatase and phosphorus levels varied considerably in cases showing no radiological changes at subsequent examinations. It is of course possible that this is a true reflection of metabolic bone changes which cannot be detected radiologically, but, since we were unable to demonstrate any correlation between radiological and biochemical changes, this is unlikely, and radiology must be considered our most reliable index of diagnosis.

CONCLUSIONS

1. Appreciable degrees of cranial softening are very common (50%) in non-European children aged 3-12 months attending the out-patient department at Groote Schuur Hospital.

2. Cranial softening can certainly occur without rickets; it does not necessarily lead to rickets, does not disappear when rickets heals, and may in fact have no relation to rickets whatever.

3. Rickets is extremely common in the patients here considered, the incidence being certainly over 30% and possibly as high as 80%.

4. Radiological evidence of rickets, although probably indicative of relatively advanced rickets, is the most reliable criterion for diagnosis and of progress. We have not demonstrated that cranial softening or biochemical changes preceded radiological abnormalities.

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APPENDIX

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AN ELECTRONIC NEONATAL RESPIRATORY MONITOR*

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To all who are concerned with the care of the newborn, and particularly of the premature baby, cyanotic and apnoeic attacks are familiar, alarming and depressing events. How often has one entered a nursery to find a 'prem', who was apparently quite well when last seen only a few minutes previously, now limp and blue, and whom one revives with considerable difficulty, only to learn of its subsequent demise in another apnoeic attack! How often is the 'cerebral' baby, whom the sister left for a few minutes to attend to another emergency, found dead on her return! How often, too, does one hesitate before demanding a special nurse for such cases, knowing that in private practice the financial strain placed upon young parents may be considerable, and that in State hospitals such staff can often not be spared! Yet there is no doubt that babies liable to apnoeic attacks should be under continuous and uninterrupted observation if avoidable fatalities are to be prevented. Such babies, if treated early in the attack, can frequently be revived by any form of simple stimulation. Timely aspiration of obstructing mucus in the nasopharynx will frequently save such a baby's life. Further measures such as oxygen administration, intramuscular, intravenous or intracardiac stimulants, or some form of artificial respiration, may become necessary if the attack is prolonged and anoxia has depressed the respiratory centre. But the basic essential in the management of such babies is the early detection of apnoeic episodes and the immediate availability of an attendant to deal with them.

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Which Babies are particularly Liable to Cyanotic Attacks?

Small premature babies are especially prone, and Illingworth[1] in his study of 170 babies who had cyanotic attacks found that 60% were premature. Miller,[2] observing the respiratory behaviour of several hundred neonates, including 229 premature babies, found that all the deaths occurred among those showing a significant rise in respiratory rate after the first hour (his group III, which contained the vast majority of small premature babies). It is generally recognized that in the management of the premature baby 'maintenance of respiration' is one of the cardinal aims.

Apart from prematurity, cyanotic attacks were found by Illingworth[1] to be associated with certain maternal antenatal conditions — toxaemia, hypertension and antepartum haemorrhage — with intrapartum foetal asphyxia (24% of the babies had initial grade-2 or grade-3 asphyxia in Flagg's classification); and in those who died the commonest findings were atelectasis (with or without hyaline membrane), cerebral haemorrhage, and cerebral oedema. Less frequent findings were infections, pulmonary haemorrhage, oesophageal anomalies, and congenital heart disease.

Cyanotic attacks should therefore be anticipated in (1) premature babies, (2) babies showing initial moderate or severe asphyxia, (3) any ill baby, particularly if atelectasis, cerebral haemorrhage or cerebral oedema is suspected, and (4) any baby showing a significant rise in respiratory rate after the first hour of life.

When are Cyanotic Attacks most likely to Occur?

Although the first 3 days are commonly stated to be

the most dangerous period from this point of view, and although it is true that the majority of attacks do occur on these days (72% in Illingworth's study[1]), nevertheless a significant number (28%) occur in the succeeding days; Miller[2] found a tendency for apnoeic attacks to occur throughout the first week. It follows that a baby in which such episodes might be anticipated should ideally have its respirations watched continuously for at least the first week of life.

The Problem

It is obviously impracticable to have every baby with a liability to cyanotic attacks 'specialled' for the first week, or even the first 3 days. If a device could be made which would alarm the attendants in the early stages of an apnoeic episode the same purpose would be fulfilled, with a great saving in personnel-hours. The apparatus should be simple, safe, reliable and inexpensive. It should be applicable to babies in incubators. It should not in any way hamper the respiration of the baby, nor should it interfere with access or observation. It should not introduce any potential danger such as infection or electrocution. Furthermore, it should be capable of distinguishing between true apnoeic attacks and the common pauses in respiration associated with periodic breathing, so frequently seen in the premature baby. These requirements seem to have been adequately met by the device here presented.

The Apparatus

The device consists of 3 units, viz.: (1) a respiratory-motion detector or transducer, (2) the respiratory-pulse integrator and alarm control, and (3) an extension alarm. Briefly, the function of these various parts is as follows:

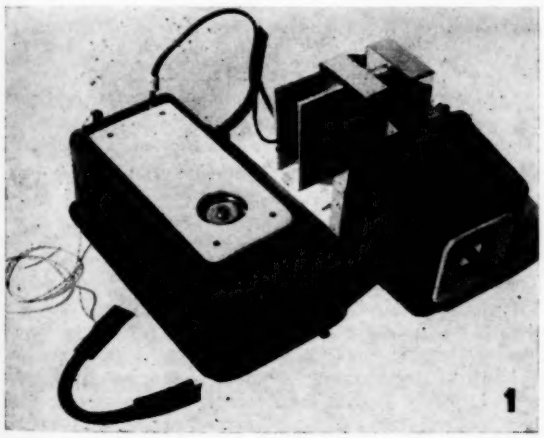

Fig. 1. The apparatus.

1. *The transducer.* This consists of a length of rubber tubing packed with carbon granules. When strapped over the baby's upper abdomen the longitudinal expansion and contraction of the tubing with the baby's respiratory movement causes a varying resistance, thereby converting mechanical variation into electrical variation. This detector plugs into:

2. *The integrator and alarm control.* The varying electric pulse developed with the aid of the detector is amplified and caused to pass to an integrating circuit, the output of which is a function of respiratory amplitude and periodicity. This pulse is used to charge a reservoir capacitor. An electromechanical switch (relay) is held in the 'off' position so long as the integrated output exceeds a certain level. Should respiratory motion cease the capacitor slowly discharges, and at the critical level the relay reverts to the 'on' position, thereby completing an alarm circuit. The apparatus is so devised that the delay period is about 15 seconds. This is to exclude 'false alarms' resulting from periodic breathing. Battery or circuit faults producing a drop in integrated output will also cause the relay to revert to the 'on' position. An alarm hooter is incorporated in the casing of this part of the apparatus.

3. *The extension alarm.* This is simply an extra hooter to extend the range of the alarm. It plugs into the main component and can conveniently be hung over a door.

The whole apparatus is battery-powered, so that no extrinsic power-supply is necessary. It is furthermore extremely light and portable.

Experience with the Apparatus

A prototype has been in use for about 6 months. Towards the end of this period some trouble was experienced with the relay, but this has been remedied in the final model. Apart from this small defect the machine showed itself to be a reliable and efficient detector of apnoeic attacks. Not once did it alarm without just cause, and on more than one occasion it detected the attack of apnoea before a trained nurse did who was simultaneously 'specialling' the baby. We have, therefore, every confidence in the apparatus.

Wherever it has been in use the alarm has been welcomed most enthusiastically by the nursing staff, who, liberated from the necessity of watching the baby every few minutes, are able confidently to get on with their routine duties. To the paediatrician it gives the considerable reassurance of knowing that the baby will not die in an apnoeic attack without having received immediate attention. And, as for our small patients, we hope the apparatus will prove instrumental in saving some of their precarious lives.

SUMMARY

An electronic device is described which will monitor the respirations of the newborn and sound an alarm should the respiratory movements cease. By its use apnoeic attacks are reliably detected in their early stages and the need for 'special' nurses to maintain the respiration of premature or ill newborn infants is obviated.

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MEDICAL AND EDUCATIONAL PROBLEMS OF THE BRAIN-INJURED CHILD*

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In order to lay down standards for admission to our cerebral-palsy schools, the Union Department of Education, Arts, and Science has accepted the following definition of cerebral palsy (drawn up by the Technical Committee of the Cerebral Palsy Division of the National Council for the Care of Cripples in South Africa): 'Cerebral palsy is a term used to designate any abnormal alteration of movement or motor function arising from a defect, injury or disease of the nervous tissue contained within the cranial cavity. The lesion may be localized or diffuse and it may be caused by factors arising before, during, or after birth'.

Among the signs and symptoms present are the following: motor dysfunction, convulsions, speech defects, mental retardation, behaviour disturbances of organic origin, and sensory losses, particularly in hearing and vision.

It is recommended that the handicapped brain-injured child without motor impairment, defined as follows by Strauss and Lehtinen be considered under certain circumstances for admission to a cerebral-palsy school: 'A brain-injured child is one who, before, during, or after birth has received an injury to, or suffered from an infection of, the brain. As a result of such organic impairment, defects of the neuro-motor system may be present or absent. However, such a child may show disturbances in perception, thinking, and emotional behaviour, either separately or in combination'.

The criteria for admission to cerebral-palsy schools are as follows:

1. All children suffering from cerebral palsy in terms of the definition of the National Council for the Care of Cripples in South Africa.

2. The children must be able to benefit by the corrective and educational treatment provided at the school.

3. The brain-injured child (Strauss and Lehtinen) may be admitted provided he can benefit by the school programme and is not aggressive.

The approach to the handicapped brain-injured child without motor impairment is essentially an original approach peculiarly applicable to South Africa. Because of the absence of facilities for educating these children, and because their educational problems are identical with the accepted types of cerebral palsy, we can assist by taking them into our schools. That this decision is a wise one is shown in our own school in Pretoria. This school has been of considerable help to children who were floundering in the ordinary schools, and who are now making good progress. The big advantage of tuition in a special school is the fact that teachers are provided on a basis of 1 to 10 pupils. As soon as a quota of 16 is reached an extra teacher is provided — this is in terms of the regulations and can be demanded as a right. Contrast this with an ordinary school where the teacher has to cope with 30 - 50 children. You can well imagine what happens to the retarded or handicapped child under such conditions.

Educational problems arising out of physical defects would not have been discussed at a medical meeting 20 or 30 years ago. The modern trend in social medicine is, however, drawing the physician, and in particular the paediatrician, into a holistic alliance — that is, into treating the child as a whole, and not merely that part of his body which is affected.

It has become important to realize that in the field of cerebral palsy it is not only the numerous medical specialists who are required to treat the handicaps, but that paramedical personnel — therapists of various types, as well as psychologists and teachers — are an essential part of the team. I would say that teachers are the most important but they are unable to carry on their difficult and complicated task without a proper diagnosis and without proper medical guidance. Hence our institutions for cerebral palsy in South Africa are called 'schools' and not hospitals, and the heads of these schools are teachers and not doctors.

A situation has therefore arisen in which medical personnel are inevitably drawn into close contact with lay people. Not only must the doctor at the cerebral-palsy school work with such people at the schools, but, if they are to complete their work in its widest implications — those of helping towards the rehabilitation of the child — they must be in close contact with the parents' associations and with the wider public who support the schools financially.

SENSORY AND MOTOR DEFECTS

This paper is restricted mainly to the sensory defects in the cerebral-palsied child, with and without motor defects, all of which interfere with his education.

Most of the material that is being presented is taken from the data quoted in *Cerebral Palsy in Childhood* by Dr. Grace E. Woods.[1]

Visual Defects

These are present in about 60% of the children, the commonest being defective eye movements (32%); a few are blind (3%); a few have defects of their field of vision (4%); and some have impaired vision (15%). The cause in most of these cases is cortical and not peripheral damage. There is cortical damage causing a defect of vision or of memory of visual imagery. The child is unable to perceive the world in three dimensions but as he gets older and is able to move about, he begins to improve and may be able to learn to judge distance, size, and texture. Many cerebral-palsied children lack binocular or stereoscopic vision; this is not always necessarily serious. The defect may be due to occipital damage causing inability to recognize pictures, shapes, and perspectives.

In *muscular imbalance*, in contrast to what occurs in simple strabismus, single muscles are not necessarily involved. The whole nature of the eye movements is at

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fault. This may correlate with the physical disability, e.g. in a severe adductor spasm the eyes may converge. The eyes may become fixed, like the joints, but if the patient relaxes the eyes may have full movements.

In the *athetoid child*, conjugate deviation of the eyes from one side to the other may be related to the persistence of a tonic neck reflex. The eyes deviate to the side of the strongest tonic neck reflex and get pulled over. In some athetoid children there is an alternating squint. Other children will look sideways, and develop an ocular torticollis. They will walk with their heads to one side and with arms and legs in a position suggestive of the tonic neck reflex. Treatment to the whole body may improve these abnormalities, but it has to be given early.

The *ataxic child* may have difficulty in holding his eyes in conjugate deviation, the eyeballs springing back to a central position. He will have difficulty in reading and walking, since he is unable to hold his eyes in the lateral position which will result in visual confusion. In addition there may be parietal-lobe damage which will add to the learning difficulty as a result of the disturbance of spatial perception, number sense, and sense of body image.

In *spasmus fixius* the head shifts from side to side in walking, even when the eye movements are normal.

In *ataxic athetosis*, due to a lesion in the superior colliculus and the cochlear nucleus, there is athetosis with very little tension, defective upper movements of the eyes, deafness, and poor head control.

Hearing Defects

These occur in 10% of the children. They are not due to peripheral or nerve deafness, but to central defects. There are two types of deafness — high-frequency deafness and auditory agnosia. High-frequency deafness is usually due to neonatal jaundice involving the cochlear nucleus. Cortical or sub-cortical lesions cause auditory agnosia. In this condition the child can hear but the sounds are meaningless. There is some specific difficulty in synthesizing sounds and breaking down words into their components. This may increase inattention to auditory stimuli.

Just as the residual hearing in deaf children can be helped if their training is commenced early in life, so can cerebral-palsied children with auditory agnosia be helped if they are taught to hear and listen, by prolonged period approach by means of auditory experience only. This teaching, however, must be started in the first year of life.

In this connection it is most important to know that the Special Schools Act which has been before Parliament makes provision for the 'admission of a child to a Special School from any age, if suffering from blindness, deafness, epilepsy, or cerebral palsy'. This is a great advance in social legislation affecting handicapped children.

Aphasia

This presents a real problem in our schools. That aphasics fall into the definition of brain-injured children must be accepted. It is this type of case that in the first instance made us widen our definition. These cases really should be taught on their own because they are a real problem in education. In most countries they are taught in schools for the deaf. In South Africa some of these schools admit them, others do not. As a result we have a number of aphasic children in our school in Pretoria who are making reasonable progress. One such child spent three years at our school, and is now attending a normal school and competing on even terms with the children there. We shall probably have to start a special class as soon as we have enough children.

Aphasia is divided into receptive and expressive types (previously known as sensory or motor). Usually both components are present. In receptive aphasia the child can hear, but he is not able to translate what he hears into meaning. The understanding of speech is located in the dominant hemisphere with a subsidiary centre in the non-dominant hemisphere. If the receptive centre of one hemisphere is damaged, the other one can be trained to take over and become dominant. This is because both centres have potential, though not altogether equal, possibilities at birth of being trained as language association systems. In expressive aphasia the child can hear and understand but is unable to speak. The defect is not due to any difficulty of the muscles of speech but is due to a lesion in the motor speech area of the cortex — the frontal lobe on the dominant side. The other hemisphere can take over the function of the speech centre if this is damaged at birth or in early life.

Speech Defects

These are mainly due to lack of motor control of the organs of speech where there is spasticity, athetosis, and ataxia of the movements of the face, lips, tongue, palate, and the organs of deglutition and respiration. The greatest difficulty is with the athetoid child.

EDUCABILITY OF THE CEREBRAL-PALSIED CHILD

Schoolchildren are classified into four main groups, the ineducable, the educationally abnormal, the normal, and those with superior intelligence.

Children who have an injury in the non-dominant hemisphere have, according to McDonald Critchley,[2] executive difficulties (they forget *how* to do things) whereas in the dominant hemisphere memory is stored and the patient with an injury here forgets *what* to do. It is thus seen that both hemispheres have important functions in learning.

Disorders Due to Brain Damage

Children with brain damage suffer from three main disorders (these do not apply to all cerebral-palsied children):

1. *Lack of concentration* with marked distractability. A number of factors may contribute towards this. They include inability to focus or discern objects; muscular spasm with loss of power to make efforts to concentrate; severe educational difficulties in which ordinary teaching methods are too difficult for the child, whereupon he ceases to attend; and epileptiform stimuli (without any fits) in which stimuli from the damaged areas may interfere with the normal functioning of the brain.

2. *Hyperexcitability*. The child has difficulty in remaining seated and shows uninhibited behaviour.

3. *Perseveration.* Here there is persistent repetition of an activity once it is begun.

The above disorders result from the disorientation of the child's cerebration and an inability to organize separate and consecutive thought.

Learning Difficulties

These are present as the result of a lowering of the general intelligence and of behaviour disorders in some children. There is evidence of perceptive and conceptual disorders which affect their ability to learn. These children are frequently labelled mentally backward but the difficulties may be due to specific brain injury.

Perception is the activity of the mind intermediate between sensation and thought. It gives a particular meaning and significance to a given sensation and acts therefore as a preliminary to thinking.

In apparently mentally-normal children who have cerebral palsy, certain learning difficulties may present themselves. These include: not understanding the difference between up and down, horizontal and vertical, right and left, round and square; inability to recognize letters or pick out objects in pictures; and difficulty in translating the three dimensions of ordinary vision into the two dimensions of pictures, with the result that the child may not be able to recognize objects.

Difficulties with numbers may be part of a general learning disability in which reading and writing are normal. The child may not know that 4 is greater than 3. He is incapable of giving the correct number of articles on request. There may be difficulty in visualizing the size of groups of pegs on a board. Such children may attend normal schools without anyone realizing the significance of the child's difficulties.

Executive side. Here the child cannot copy simple lines, slanting lines, angles and shapes. The child may be able to read but writing is difficult. He may not be able to copy words but is able to write words or stories voluntarily. There may be mirror writing or upside-down writing. Drawings may be disorientated with the wrong proportions. The child may be incapable of making any organized shapes. These perceptual difficulties may be related to some definite clinical signs.

Sensory discrimination. There is no marked relationship between astereognosis and perceptual difficulties. Some hemiplegic children with astereognosis have no learning difficulties and some with learning difficulties have no astereognosis. In some, both co-exist.

Crossed-lateralism is difficult to assess as a cause of learning difficulties. Children with this defect may indulge in mirror-writing, reversal of words or numbers, and reversal of the direction of writing. These are considered to be minor sources of difficulty.

Body image. With these perceptual difficulties we must associate the difficulty in conception of the shape of the body and its position in space — that is, appreciation of the body image. Ritchie Russell[3] defines the body image system as that which makes it possible for appropriate bodily movements to be performed in relation to apparent stimuli.

The development of the body image is fundamental to normal development and behaviour as by this means we are in a constant state of awareness of the position of the body. Lesions in the parietal and occipital lobes of the non-dominant hemisphere may result in interference with the normal development of the body image. McDonald Critchley[2] describes difficulties in adults. In children this defect may produce great learning difficulties because the child may not be able to distinguish between right and left, or to recognize pictures. There is difficulty in calculation and in the execution of letters. Gerstmann's syndrome, the lack of ability to recognize covered fingers, may result in arithmetical difficulties, because the ability to count on 10 fingers and 10 toes is basic to one's conception of numbers.

CONCLUSION

In summing up I should like to recapitulate some of the essential difficulties with which a brain-injured child may be confronted in his education. They are: mild or severe difficulty in learning the three Rs, recognition of shapes, and execution of shapes; difficulty with numbers; and lack of body image (some may have the feeling of floating in space, without focussing, understanding, or coordinating their activities). Some brain-injured children have none of these difficulties.

The parts of the brain that dominate the picture in the education of the brain-injured child are:

1. The *parietal lobes* controlling perception, body image, and finger agnosia.

2. The *temporal lobes* controlling behaviour.

3. The *occipital lobes* controlling spatial behaviour.

It is the total cerebral damage that determines the learning capacity of such a child.

I have tried to present a picture of the many difficulties facing a cerebral-palsied child in his struggles in life. Being neither a teacher nor a neurologist, I have not been able to present as composite a picture as the subject deserves. I have drawn on information gained from Dr. Grace Woods,[1,4] Mme. Stella Albitreccia[5] and Sir Ritchie Russell,[3] whom I met at the last meeting of the International Study Group on Child Neurology and Cerebral Palsy held at Oxford in 1958. I have also had contact with this problem at our cerebral-palsy school in Pretoria. These difficulties are real, and present a great challenge to teachers and doctors.

An important contribution to the knowledge of this subject will be research into the normal and abnormal development of the human infant from the moment of birth. Our greatest asset will be early and correct diagnosis of brain injury in patients who can describe no symptoms, and show minimal signs or none at all, a concept which at present is difficult to visualize.

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THE TREATMENT WITH FUROXONE OF SALMONELLOSIS IN INFANTS AND CHILDREN

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A significant number of cases of salmonellosis are resistant to treatment with antibiotics.[1,2] The unpredictable but frequent temporary or permanent disappearance of salmonella from the gastro-intestinal tract during the natural course of the disease adds to the difficulty of assessing antibiotic therapy. It is also often difficult to secure from treated patients an adequate series of specimens for culture after recovery from the acute illness.

Furoxone [3-(5-nitrofurfurylideneamino)-oxazoldin-2-one] has been suggested as a preparation which might offer an important advance in the treatment of salmonella infection.[3-5] It has been used in veterinary medicine since 1952 and a related compound, nitrofurantoin (furadantin), is in current use for the treatment of infections of the urinary tract. After oral administration to human subjects, bacteriological and spectrophotometric assays show that up to 9% of furoxone remains in the faeces and 2-8% appears in the urine. The remainder is presumably catabolized by bacteria in the intestine and by the tissues after absorption.

Various workers[3-5] reported furoxone to be a potent and effective bactericidal agent at low concentrations, and active against many enteric pathogens including salmonellae, shigellae, and *Staphylococcus aureus*. Bacterial resistance developed slowly, and organisms resistant to furoxone were not cross-resistant to penicillin G, streptomycin, chloramphenicol, chlortetracycline, and oxytetracycline.[3]

In 2 published series[6,7] 87·5% and 91·7% of cases of salmonellosis were cured by furoxone. This paper presents the results of a trial with furoxone in the treatment of intestinal salmonella infection in a group of children aged 1 - 36 months.

Material and Method

In 19 in-patients, positive salmonella cultures were obtained from rectal swabs during the trial period. The admission diagnosis, age, salmonella typing and sensitivity tests are given in Table I. The average age of the group was 9·4 months (range 1 - 36 months), the majority of the children being under 1 year old.

All the cases, with the exception of one (R.D.), were treated with sulphonamide or broad-spectrum antibiotics for varying lengths of time before therapy with furoxone was commenced

TABLE I

Name	*Age (months)*	*Admission diagnosis*	*Pre-furoxone treatment*	*Salmonella Type*	*Sensitivity tests of culture*							*Furoxone mg./lb./24 hours*	*Duration of treatment (days)*	*Outcome of treatment*
					Chloromycetin	*Neomycin*	*Streptomycin*	*Terramycin*	*Sulphas*	*Kantrex*	*Furoxone*			
W.K.	16	D + V	Sulphonamide 7 days	B	+		+	+	+			19	7	ST
J.T.	36	D + V	Chloromycetin, Neomycin } 5 days	E_1	+		+	+	−			15	7	STF
B.S.	3	D + V	Sulphonamide 4 days	C	+	+	+	+	+	+		8	7	ST
S.M.	5	D + V	Chloromycetin 8 days	E_1	−		+	+	−			8	5	STF
K.F.	9	D + V	Chloromycetin 9 days	E_2	+		+	+	−			13	6	ST
R.D.	12	D + V	—	B	+		+	+	+			19	6	STF
V.S.	2	D + V	Neomycin, Erythromycin } 6 days	B	+		+	+	−	−		6	7	F
Vic.S.	2	D + V	Dysentil 6 days	B	+		+	+	−	−		6	7	F
H.H.	1	D + V	Albamycin, Neomycin } 5 days; Sulphonamide 7 days, Sulphadiazine 4 days	C_2	+		+	+				15	10	F
Y.S.	14	D + V	Chloromycetin 5 days, Terramycin 6 days	UI	+		+	+				7·5	7	F
I.G.	20	D + V	Sulphonamide 3 days, Sulphas 5 days	B	+	+	+	+	−	+	+	20	3	STF
R.W.	4	D + V Staph. pneumonia	Chloromycetin 11 days, Albamycin, Erythromycin } 13 days	UI	±		±	±		+	+	6	6	F
P.M.	4	Salmonella meningitis	Chloromycetin, Sulphas, Streptomycin, Penicillin, Terramycin } 21 days	E_1	+		+	+	+	+		15	7	F
D.P.	3	Pyloric stenosis	Chloromycetin, Neomycin } 6 days	B	+	+	+	+	+	+		10·5	6	F
A.R.	1	Urinary infection	Chloromycetin 7 days	B	+		+	+	−		+	14	6	ST
I.B.	7	Broncho-pneumonia	Chloromycetin, Streptomycin } 6 days	C_2	+		+	+	−	+	+	9	6	F
E.C.	5	D + V Br.-pneumonia	Chloromycetin 7 days	C	+		+	+	+			50	7	F
P.S.	8	D + V Br.-pneumonia	Sulphonamide 4 days	C_1	+		+	+	−		+	10	7	F
A.R.	26	Kwashiorkor	Dysentil 7 days	C_2	+		+	+	−			10·5	13	F

All the salmonellae were insensitive to penicillin, erythromycin and novobiocin.

D + V = diarrhoea and vomiting. UI = Unidentifiable. ST = Successful therapy. STF = Successful therapy with furoxone. F = Failure—persistence of infection.

(Table I). Rectal swabs were obtained for culture in all cases immediately before treatment with furoxone. Further rectal swabs were taken at intervals and cases were regarded as cured only if 3 or more consecutive rectal swabs were negative on culture.

Furoxone suspension (1 drachm = 50 mg.) was given in higher dosage than advised by the manufacturers (2·5 mg. per lb. body-weight over 24 hours). The doses given varied between 6 and 50 mg. per lb. body-weight in 4 divided doses over 24 hours, the average being 14 mg. per lb. body-weight. The duration of therapy varied from 3 to 13 days, the average being 6·8 days. Two cases, S.M. and I.G., were on intravenous fluid therapy for 5 and 3 days respectively.

Results

Of the 19 cases, 4 were cured by sulphonamide or chloromycetin, but this was not known at the time of starting the administration of furoxone. The efficacy of furoxone treatment was therefore assessed in the 15 remaining cases. Three or more consecutive rectal swabs negative on culture were obtained in 4 cases (26·7%). In 11 cases (73·3%) positive cultures for salmonella were still obtained after the furoxone therapy. These cases, therefore, proved resistant to furoxone, sulphonamide, and the antibiotics employed (Table I).

By the time therapy with furoxone was commenced, the character of the stools in the majority of cases was relatively normal. In none of the children was the presence of blood and mucus reported by the mother or nursing staff. In the cases with frequent loose stools, these were described as watery, yellow or greenish. The average numbers of stools per day before and after therapy were 4·3 and 3·0 respectively for the group.

An average weight gain of 7·1 oz. (gain in 10 cases, no gain in 2, and loss in 3) was recorded over the average period of 6·8 days of treatment. The majority of cases, however, were already gaining weight before therapy with furoxone was begun.

The side-effects of treatment with furoxone are said to be nausea and vomiting. In none of the 5 patients who vomited during the period of therapy was it thought to be due to the furoxone. Even in E.C. (aged 5 months), where a dosage of 50 mg. per lb. over 24 hours was given for 7 days, no untoward effects were noted. In all patients on furoxone therapy the urine became dark yellow within 2 - 3 hours of taking the drug.

Discussion

In the present series 73·3% of cases of salmonellosis resistant to therapy with sulphonamide and antibiotics also proved resistant to therapy with furoxone. The results, then, in this particular age-group (average 9·4 months) are disappointing and not in agreement with those of other workers.[6,7]

Factors other than drugs may play a part in the successful therapy of salmonellosis. Although the numbers are too small to draw definite conclusions, it is interesting to note the different ages in the present series. The average ages of the groups cured by sulphonamide and chloromycetin on the one hand and furoxone on the other (13·5 and 14·6 months respectively) are much higher than the average age (4·45 months) of the group resistant to antibiotics and furoxone. There was no significant difference in the average dosage of furoxone in the groups which responded to therapy and which failed to respond (13·2 mg. and 14·6 mg. per lb. body-weight respectively).

Sensitivity tests on the salmonellae cultured were carried out in 5 cases. Although all 5 were reported as sensitive to furoxone, in only one of them (I.G.) did the stool culture become negative (Table I).

The majority of cases of gastro-enteritis admitted to the wards are undernourished and show multiple pathology and often associated parenteral infection. Experience in 2 cases in the present series, and unpublished data in cases of acute gastro-enteritis other than salmonellosis, suggest that these cases when treated with furoxone require additional antibiotic therapy. The antibiotic employed, while perhaps unable to suppress the excretion of viable salmonella, affords some protection against the systemic effects of the infection and may prevent a lethal outcome.

SUMMARY

Fifteen cases of salmonella enteritis were treated with a new preparation, furoxone. The results in the particular age group were disappointing; in 11 cases (73·3%) positive cultures for salmonella were obtained from rectal swabs after a course of furoxone therapy.

I wish to thank Prof. F. J. Ford for his encouragement and advice, and Dr. J. G. Burger, Superintendent, Groote Schuur Hospital, for permission to publish. I am grateful to SKF Laboratories (Pty.) Ltd. for supplying furoxone suspension. Drs. S. Esrachowitz, B. Goldschmidt and G. Wittmann cooperated in the trial. The assistance given by the Department of Bacteriology, Medical School, University of Cape Town, is appreciated.

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SOUTH AFRICAN PAEDIATRIC ASSOCIATION (M.A.S.A.)

SUMMARIES OF SCIENTIFIC PAPERS*

1. THE HEART IN KWASHIORKOR

DRS. P. M. SMYTHE, A. SWANEPOEL and J. A. H. CAMPBELL, *Cape Town*

The purpose of this paper was to describe in detail the serial changes found in the ECG and X-ray of the heart during the recovery phase of kwashiorkor; to investigate the possible rôle of the heart in fatal cases of kwashiorkor, and to consider the possibility that in kwashiorkor some changes might be found that would help to explain the changes associated with the so-called 'nutritional heart' of the adult Bantu.

X-rays taken on admission were examined for heart size and showed a significant decrease in the transverse diameter of the heart when compared with a normal control series. Serial X-rays during recovery showed a consistent increase in heart size. An early and rapid increase in heart size was thought to be due to an increased venous return, while a later and slower increase might have been due to an increase in muscle bulk of the heart associated with protein repletion.

The ECG changes were arbitrarily classified into 5 groups: ionic; sharp T inversion; low voltage and flat T; a striking series of changes that occurred during convalescence; and cold injury. The changes which occurred during convalescence have been called the 'recovery pattern'; some of these had not previously been described.

There were 28 fatal cases in which the ECG changes were classified in the same way as those of children who recovered. In these the ionic type of ECG correlated well with the serum-potassium levels as did those with low voltage and flat T waves. A unique case showed a pattern of anterior transmural infarction.

In 75% of the fatal cases an adequate cause of death, other than heart disease, was found at autopsy. In the remaining 25% of cases in which no satisfactory cause of death was demonstrable there was no clearly defined histological change to indicate heart disease as the cause of death. With 2 exceptions there was no correlation between the ECG and the autopsy findings.

Some of the hearts were very small, suggesting that atrophy occurred, while in other hearts there was a pathological increase in weight which histological examination suggested was due to oedema.

Changes were found in some infants' hearts that were histologically similar to those described in the so-called 'nutri-

* Papers presented at the Fourth Congress of the South African Paediatric Association (M.A.S.A.), Cape Town, 4 - 6 April 1960.

tional heart' of the adult Bantu. It was stressed that this does not establish a common aetiology or pathogenesis.

These findings suggested, however, that there was some relation between 'kwashiorkor heart' and the adult type of 'nutritional heart'. So also did the ECG changes found during the recovery phase, which in some children were strikingly similar to those described in the adult Bantu 'nutritional heart'.

2. CARBOHYDRATE METABOLISM IN KWASHIORKOR

DRS. D. SLONE, L. S. TAITZ and G. S. GILCHRIST, *Johannesburg* †

Hypoglycaemia had been shown to be a cause of death in severe protein malnutrition in childhood.[1]

The aim of this study was to investigate aspects of carbohydrate metabolism in kwashiorkor by estimating the fasting blood sugar in 20 cases of kwashiorkor and in control subjects. In addition intravenous glucose-tolerance tests were performed on 9 cases of kwashiorkor.

It was shown that the fasting blood-sugar levels in patients with kwashiorkor were, on an average, 20 mg. per 100 ml. lower than the normal controls studied. Fasting blood sugar levels ranged from 10 mg. to 70 mg. per 100 ml. Intravenous glucose-tolerance tests demonstrated mild glucose intolerance. This was shown by the fact that in 8 cases glucose levels had not returned to fasting levels 120 minutes after loading. In no case was the intolerance marked enough to fulfil Duncan's criteria for diabetes mellitus.

It was postulated that defective gluconeogenesis was responsible for the occurrence of hypoglycaemia in kwashiorkor. It had been observed that in the early phase of treatment with milk, kwashiorkor patients had transient increased levels of serum amino-acids[2] and unusually low plasma-urea levels. This suggested that there was a temporary block in the deamination of amino-acids, and a consequent inability to maintain normal levels of blood sugar in the presence of a glycogen-depleted liver, under fasting conditions (8 hours).

In view of this observation it was recommended that during the first week of treatment of kwashiorkor, carbohydrate be added to the high protein feed.

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† Paper read at the Congress by Dr. L. S. Taitz.

3. THE RELATION OF RECENT RESEARCH TO THE TREATMENT OF KWASHIORKOR **

DR. J. D. L. HANSEN, *Cape Town*

The relationship of low-protein diets to the incidence of kwashiorkor was now well established. Research from many different parts of the world had also indicated the severe degree of protein depletion in this syndrome.

An important question during the last 10 years had been — did diets low in protein lead not only to protein depletion but also to disturbances of nitrogen metabolism that might under certain circumstances increase the protein depletion still further? The question was relevant because for every case of kwashiorkor there were at least 100 cases of underlying protein malnutrition. Research on the characteristics of nitrogen metabolism in cases of kwashiorkor had been necessary to provide data for the improvement of therapy and prevention.

Until 1953 there were no reports of nitrogen-balance studies done specifically on cases of kwashiorkor. Previous work on malnourished marasmic European and American children indicated that these children retained nitrogen more efficiently than normal children. In 1953 Bray[1] found that malnourished West African children retained nitrogen more efficiently than normal American children aged 7 - 9 years in spite of a higher faecal nitrogen output.

Nitrogen-balance studies on cases of kwashiorkor in Cape Town and elsewhere had now established that retention of nitrogen in cases of kwashiorkor was as efficient as that in a healthy newborn infant and far greater than that of normal children of the same age. There was thus no evidence of a breakdown in protein synthesis in cases not complicated by overt infection. There was some decrease in the absorptive capacity of the gastro-intestinal tract and an apparent susceptibility to attacks of severe diarrhoea. The diarrhoea could lead to great loss of water, nitrogen, and electrolytes, and was a significant factor in mortality. In treatment, therefore, attention had to be paid to correction of losses from the gastro-intestinal tract. Protein in the form of milk should be administered as soon as possible, in order to institute recovery and prevent further protein depletion.

On the preventive side, evidence was accumulating that merely improving the quality of low-protein cereal foods such as maize, e.g. by the addition of synthetic amino-acids, was not sufficient. Increase of total protein intake among children who were susceptible to kwashiorkor was even more important. This could best be done by the addition of animal protein to staple cereal diets but suitable mixtures of vegetable protein were also effective.

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4. KWASHIORKOR AND CULTURAL CHANGE

MISS A. MOODIE, *Cape Town*

Kwashiorkor was widely distributed and occurred under different circumstances among different populations. It had long been recognized that, although a deficiency of protein foods was the cause of kwashiorkor, this deficiency itself was attributable to a variety of social and environmental factors. The suggestion was made that cultural change rather than cultural custom was the common factor wherever kwashiorkor occurred and that the disease was a manifestation of failure by some populations to adapt to the new ways with which they were rapidly being brought into contact.

Important among these were the conditions of urban living, the growth of industry, the breakdown of old patterns of family and community life, the employment of women, and the changed set of values resulting from a money economy. The universal trend away from breast-feeding well illustrated a change in cultural habit before a satisfactory alternative was understood or economically possible. Figures were shown to illustrate the significance of early weaning in kwashiorkor.

Examples were also drawn from 3 areas in varying stages of sophistication to show the effect on nutrition of different cultures in a state of flux. Kampala, with late incidence of kwashiorkor, exemplified the effect of social disorganization on a primitive rural people without great poverty, and Trinidad, with very early kwashiorkor, the effect of ignorance in a more sophisticated and technically advanced setting. Cape Town lay mid-way, with poverty, in addition to the ignorance and disorganization which were typical of a country in the early stages of industrial development. An added complication was the recent impact of the African culture on that of the Cape Coloured and the introduction of a cheaper labour force. Kwashiorkor was widespread and seemed to be occurring at increasingly early ages in the Cape Town area as it did in Johannesburg.

It was questionable whether any cultural change was reversible in view of its symbolic value to the populations concerned.

5. COXSACKIE MYOCARDITIS

PROF. J. G. A. DAVEL, *Pretoria*

Infection of young children by members of the Coxsackie virus group appeared to be very prevalent in South Africa and caused much illness in young children. Its severity ranged from quite a mild illness to a most serious fulminating disease ending in death. Sporadic cases occurred at any time of the year but every now and then the infection assumed an epidemic form. An epidemic occurred in Pretoria during October and November 1959, and formed the subject of this report.

Previous reports during the past 6 years stressed the danger of this infection to the neonate. Montgomery *et al.*,[1] Javett *et al.*,[2] Suckling and Vogelpoel,[3] etc., described epidemics of myocarditis occurring in lying-in institutions in

various centres in Southern Africa. From these and other reports, the causative agent appeared to belong to the Coxsackie group-B viruses, types 2 - 5 being implicated, although in some, the evidence might be deemed to be inconclusive.

During October and November 1959, a number of cases occurred in Pretoria, the patients being in the older age group (5 months - 5 years) with a distressingly high mortality rate; those who died did so from a fulminating myocarditis with acute heart failure, where all manner of treatment was of no avail; others, especially the older ones, responded well, and quite quickly, to treatment.

The children were admitted to hospital after a shorter or longer period of illness which, in most of them, had been diagnosed as sore throat or upper-respiratory-tract infection with acute bronchitis of bronchopneumonia. A few patients presented with signs of heart involvement.

On admission the clinical findings included fever, injected throat, non-productive cough, tachypnoea and signs in the lungs varying from scattered râles to crepitations at both bases. A few of the more severe cases had signs of acute heart failure, e.g. marked distress, tachycardia, dyspnoea, cervical venous congestion, cardiomegaly, gallop rhythm, poor heart tones, occasional soft apical murmurs, and a rapidly enlarging painful liver. Patients, less seriously ill on admission, soon developed these signs in the wards. In none were there signs of central-nervous-system involvement, the lungs and the heart bearing the brunt of the infection.

Treatment consisted of supportive measures, putting the patients in oxygen tents, control of pyrexia and restlessness, rapid digitalization, and antibiotics. Cortisone was given in some of the cases with no effect.

Postmortem examinations were carried out in several of the fatal cases. The changes in the myocardium were identical with those shown to be due to Coxsackie group-B type 3 virus in a report from Johannesburg[2] of an epidemic in the newly-born.

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6. FANCONI'S ANAEMIA AND ITS TREATMENT

DR. R. MCDONALD, *Cape Town*

This uncommon condition of pancytopaenia with associated congenital defects was first described in 1927 by Fanconi.[1]

Numerous defects had been recorded, the commonest being hyperpigmentation, abnormalities of thumbs, microphthalmia, hypogonadism, and hyper-reflexia. These were noticed in infancy but anaemia was usually not apparent until the child was a few years old, though there were exceptions to this. Boys were affected more often than girls and the condition might be familial or sporadic. No treatment had, until recently, been effective and death had occurred within a few years of the onset of the anaemia.

Three cases in a family were described, the condition being recognized only when the third member came to hospital. This was an overt case. It was then possible to diagnose (in retrospect the condition in the eldest child who had died, and to do so as well in the second member of the family, who was admitted to hospital again for fuller examination.

As the result of an encouraging article by Shahidi and Diamond from Boston, USA,[2] the 2 surviving affected members of the family were then put on the recommended daily treament of testosterone, 2 mg. per kg.; and 10 mg. of prednisone.

In both cases preliminary results were encouraging. The elder child, who had previously required blood transfusions every 2 months, had gone for 3 months without transfusion and at the end of this time her haemoglobin was higher than on any of the previous recordings. Her platelets and granulocytes were also increasing in number and the previously hypocellular marrow was showing well-marked activity.

The younger child, with more congenital defects but less anaemia, also showed a good response to treatment. Side-effects of the drugs were, however, becoming prominent and it was therefore decided to halve the dosage of each drug.

It was still too early to forecast the ultimate fate of these children, since the treatment would have to be continued for several months, and it was not known whether further courses of treatment would then be necessary. It was, nevertheless, to be hoped that there might now be a prospect of cure for *some* patients suffering from this hitherto fatal disease.

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7. DOMICILIARY CARE OF PREMATURE INFANTS

DR. I. ROBERTSON, *Cape Town*

The results of an 18 months' experiment in the domiciliary care of Coloured and Malay premature infants born and nursed at home were presented, compared with a control group of similar infants born at home and admitted to a hospital premature unit. There was no selection of cases, domiciliary care being provided for those for whom no accommodation was available in hospital.

The mothers were lent metal cribs which were fitted with padded linings containing pockets for hot-water bottles. One of the Health Department nurses visited the homes as often as she was able in the course of her usual duties (2 or 3 times a week for 1 - 2 months), and was thus able to do special supervision of the care and feeding.

The results obtained in this series of cases were very good in all cases where the mothers were cooperative, even where housing conditions were poor. Thirty cases were cared for at home in this way and were compared with 86 admitted to hospital. The neonatal deaths were comparable, but of the 50 hospital cases who survived the first week, gastro-enteritis and bronchopneumonia were responsible for the deaths of 3 infants between 1 and 4 weeks, and 7 infants between 1 and 7 months. Of the 26 domiciliary infants who survived the first week, only 2 subsequently died of the above infections.

When weight gains were compared it was found that infants in the domiciliary series kept closely to their expected gain, whereas in the hospital series half the children fell well below their expected gain, due to a combination of frequent infections and marasmus.

The principal factors in favour of domiciliary care as brought out by this experiment were: The importance of the mother-child relationship being maintained from the start, which gave the infant continuity of care in the same environment, as well as developing in the mother a sense of responsibility and a knowledge of infant care and feeding; and the elimination of the marked susceptibility to infection displayed by the premature infants in the hospital series, both in hospital and after their return home.

If this method were adopted as a hospital out-patient service there might be a great saving in the large amount of money spent at present on the purchase of incubators and the maintenance of premature units.

8. CYSTIC DISEASE OF THE LUNG

MR. W. L. PHILLIPS, *Cape Town*

Cystic disease of the lung had evoked the interest of clinicians for a long time. It might be classified into congenital and acquired cystic disease.

Congenital cysts might be of bronchogenic or gastrogenous origin, while acquired cysts might belong to 2 sub-groups. These were (1) The various types of air cysts known as pneumatoceles, or emphysematous bullae, plus a variety of multiple cysts which resembled very closely the condition of saccular bronchiectasis; and (2) healed abscesses — it was a remarkable fact that many children who had suffered from an acute lung abscess or any staphylococcal infection of the lung were left with a residual lung cyst.

Clinically, pulmonary cysts were of 3 varieties: (1) Air-containing cysts — such cysts were in communication with the

bronchi, or had been in the past; (2) fluid-containing cysts — these cysts had usually been shut off completely from both bronchial and alimentary tract connections, and the lining wall had secreted the fluid; and (3) pus-containing cysts — these were secondarily-infected fluid-containing cysts which might show an area of surrounding pneumonitis.

Lung cysts might present in 1 of 3 ways: (1) Accidental discovery — these cysts were usually discovered accidentally on routine X-ray examination of the chest; (2) respiratory distress — an expanding lung cyst would cause respiratory distress as the lung became compressed, showing signs of respiratory embarrassment; and (3) acute lung infection — the presence of super-added infection would alter the picture, and the patient might present symptoms of acute pneumonia, of lung abscess, or of recurring attacks of acute bronchitis.

The treatment of cystic disease might be divided into emergency, medical and surgical treatment.

Emergency treatment. Expanding lung cysts required simultaneous cyst and pleural cavity drainage.

Medical treatment. Acute infections and associated empyemata, of course, had to be drained. The causal organism had to be isolated and its sensitivity to antibiotics established. The necessary antibiotics then had to be administered.

Surgical treatment. Full investigations had to be completed, since they would determine the type and extent of operation which was curative. The results of surgical resection of the affected part had been uniformly good.

9. SPIROMETRIC STUDIES IN CHILDREN

DR. H. DE V. HEESE, *Cape Town*

The evaluation of disability and the immediate and long-term assessment of pulmonary diseases, such as asthma, posed important problems for the clinician. The forced expiratory volume (FEV) and the forced vital capacity (FVC) test could be employed in the objective assessment of the disability in children resulting from common chest diseases and the reversibility of such diseases. It was a simple, interesting, easily performed and repeatable test.

The FVC was the maximum volume of gas which could be expired following a maximum inspiration, the expiratory phase being accomplished as rapidly and as forcibly as possible. The FEV was that volume of gas expired between 2 stated times during the performance of the forced vital capacity test. The time interval was indicated by a subscript, thus $FEV._{.75}$ referred to the volume expired during the first three-quarters of a second.

The $FEV._{.75}$ and FVC could be measured from the spirographic tracing of the FVC on a fast-moving kymograph using a Bernstein-type spirometer. This was termed the forced expiratory spirogram (FES) and the form and details of the FVC then became clearly visible. The FESs for a given child were in general remarkably uniform in shape and almost specific at any particular occasion for that individual. The first phase of expiration was always recorded as an almost straight line. As the speed of expiration lessened, the curve deviated from this initial straightness and became horizontal when the forced expiration was completed. In asthmatics, in proportion to the severity of the disease, the initial drop in the curve became progressively less steep, the shape being that of a shallow curve rather than an almost straight line. The time over which the FVC was expelled was prolonged.

The change in the shape of the FES of an asthmatic child after giving a bronchodilator drug such as isoprenaline, indicated the presence of reversible bronchospasm. This change, to be regarded as significant, had to result in an increase of at least 10% in the $FEV._{.75}$ and FVC values, and the absolute increase in these values had to be 50 - 75 ml. or more in volume. The likelihood of successful bronchodilator, steroid or other therapy could be assessed, as could the possible benefit or uselessness of a particular drug to any particular individual.

The severity of the bronchospasm in an asthmatic patient was reflected in the lowered absolute values for the $FEV._{.75}$ and FVC, the former being the most useful single spirometric index of ventilatory function. These values could be compared with the 'normal' expected $FEV._{.75}$ and FVC for the individual, using prediction formulae.[1] In patients with an obstructive defect (asthma and emphysema) the $FEV._{.75}$ was lowered to a larger extent than the FVC, and when expressed as a percentage (FEV%) of the FVC might fall to very low levels. In a patient with asthma, therefore, a low value for the $FEV._{.75}$% suggested insufficient treatment or the presence of concurrent emphysema. Serial readings helped to distinguish these two.

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10. PATHOLOGY — AIDS TO DIAGNOSIS IN PAEDIATRICS

DR. D. MCKENZIE, *Cape Town*

This paper was in the nature of a review of the more common diseases of children encountered at the Red Cross War Memorial Children's Hospital, Cape Town, and the part the laboratory played in diagnosis.

The biggest problem encountered was that of gastro-enteritis and in the summer season 9,000 cases were seen, 1,200 requiring intravenous resuscitation. Only 200 stools and rectal swabs were cultured, so the coverage of these cases was small; however, 5·7% of specimens yielded salmonellae and 2% shigellae. At an outside clinic a single investigation yielded 17% shigellae and 3% salmonellae, illustrating the difference between clinic and hospital practice. The cause of death in 6% of cases coming to autopsy was salmonella or shigella infection. Attention was drawn to the biochemical imbalance in these cases resulting in hyperosmolaric, hypoglycaemic and hyperglycaemic states and their sequelae.

The frequency of parasitic infestation even in the very young was stressed and attention drawn to the surgical complications of ascariasis and the medical syndromes following infestation with *Giardia lamblia*, which were relatively common.

The value of duodenal intubation in giardiasis and in fibrocystic disease was indicated and newer methods of assessing malabsorption states were evaluated. Four out of 8 autopsies on patients with fibrocystic disease were in Coloured children.

The difficulties encountered in the differential diagnosis of jaundice of the newborn were discussed, in particular the differentiation of biliary atresia from neonatal hepatitis. The use of serum-transaminase levels as a guide had not proved diagnostic in any way but might sometimes be of value.

The problems of disseminated herpes simplex virus infection and Hirschsprung's disease were indicated. Examination of frozen sections of biopsy material were of considerable aid to surgeons in the treatment of Hirschsprung's disease.

The great value which accrued from the close cooperation between clinicians and pathologists, when the laboratory was situated in the hospital building, was stressed. This ideal situation resulted in a better service for the patient and a more direct control of such problems as cross-infection, sterilization and the overall therapeutic policy of the hospital.

11. THE COLLECTION OF SPUTUM IN CHILDREN WITH A DESCRIPTION OF A NEW TECHNIQUE

DR. I. MIRVISH, *Cape Town*

Valuable information could be obtained by bacterial examination of the sputum, e.g. in tuberculosis, pertussis, and other lower respiratory infections. The collection of sputum in young children, however, was rendered difficult by the fact that children under 6 years of age tended to swallow their sputum instead of coughing it up.

Procedures used in the collection of sputum were discussed and evaluated in the paper and a new technique was described, referred to as supralaryngeal aspiration.

The procedures described included gastric lavage, the 'cough swab', the larvngeal swab or supralaryngeal swab, and the serum swab. Gastric lavage was essentially a hospital procedure, and 'cough swabs' collected only small quantities of sputum.

The principle of the new technique (supralaryngeal aspiration), was to promote a bout of coughing and aspirate the sputum produced into a tube, instead of catching it on a swab. The apparatus consisted of a glass medicine or vitamin dropper, preferably one with an angled end, to which was attached 3 inches of thin plastic tubing. (The tubing used in the Baxter intravenous sets was eminently satisfactory.) A large rubber bulb was substituted for the small bulb usually present. The prepared set could be sterilized by inserting it into a wide test tube and autoclaving it.

The method was as follows: With the child lying down and held firmly, a wide spatula was introduced to depress the tongue, and the soft tubing was pushed down to just above the glottis, while the bulb was squeezed between the forefinger and thumb. As a result of this manoeuvre, a fit of coughing was produced, and when the bulb was released some coughed-up sputum was aspirated into the tube. With experience, about a quarter- to a half-an-inch of thick tenacious sputum was aspirated into the tube.

The advantages of this technique were, that the apparatus was simply made and easily manipulated, the soft tube was not likely to cause trauma, the procedure could easily be carried out at home or at the clinic, and sufficient sputum could be collected for direct examination, guinea-pig inoculation, and culture.

A preliminary trial at the Dr. A. J. Stals Memorial Sanatorium, Cape Town, suggested that the technique was useful. Further work was proceeding.

12. RHEUMATIC FEVER IN CAPE TOWN: A COMPARISON OF TWO FORMS OF THERAPY

DR. C. RAINIER-POPE, *Cape Town*

The results of 2 forms of therapy in patients suffering from rheumatic fever were reported.

During the 18 months following the opening of the Red Cross War Memorial Children's Hospital, Cape Town, salicylates only were used in the treatment of rheumatic fever. Thereafter high dosage steroids (prednisolone) together with salicylates were used in accordance with the scheme advocated by Illingworth *et al.*[1] in 1957.

All patients included in the survey had to conform to the modified Duckett Jones criteria[2] for the diagnosis of rheumatic fever.

There were thus 2 groups of patients, 18 cases treated with salicylates only, and 28 patients treated with high dosage steroids and salicylates. All patients were seen regularly after discharge and their cardiac state was reviewed 2 years after their last attack of rheumatic fever.

The results of the survey showed that in the salicylate group 29·4% of new cases had established heart disease 2 years after their last attack. In the steroid and salicylate group, 31% had cardiac damage after 2 years.

The second finding was that in patients treated with steroids, the ESR fell to normal extremely rapidly. Only 1 out of 25 patients had a raised ESR 3 weeks after treatment was started. In the salicylate group, however, 7 out of 11 patients had a raised ESR at 3 weeks.

The series was too small for definite conclusions to be drawn. However, the incidence of cardiac damage in patients treated with salicylates was very low in comparison with the generally reported results, e.g. 60% in patients reported both by Bland and Jones[3] and by the 1955 cooperative trial.[4] Long-term follow-up in the 2 groups was much the same.

However, in patients treated with steroids the fall in ESR and the rapid return to health was very striking. The length of invalidism and stay in hospital was much reduced. If the fall in ESR was indicative of a cessation of the rheumatic process, obviously this form of therapy was very desirable.

A plea for further investigation and accurate diagnosis of rheumatic fever was made.

1. Illingworth, R. S., Lorber, J., Holt, K. S. and Rendle-Short, J. (1957): Lancet, **2**, 653.
2. Jones, T. D. (1944): J. Amer. Med. Assoc., **126**, 481.
3. Bland, E. F. and Jones, T. D. (1952): Ann. Intern. Med., **36**, 1006.
4. Cooperative Clinical Trial (1955): Brit. Med. J., **1**, 555.

13. PURULENT MENINGITIS

DR. S. R. ESRACHOWITZ, *Cape Town*

There had been much controversy over the treatment of non-tuberculous meningitis, and no satisfactory single antibiotic or combination of antibiotics had proved ideal, whether given parenterally or orally only, or in combination with intrathecal therapy.

At the City Hospital for Infectious Diseases, Cape Town, 306 cases were seen over a 3-year period from January 1955 to December 1957. These were divided into 4 main groups.

In the first group, meningococcal meningitis, there were 198 patients (65%), including adults. Routine treatment consisted of penicillin and sulphonamide, with chloromycetin given only in severe cases. In addition, penicillin and/or chloromycetin were given at the initial lumbar puncture. Patients with the Waterhouse-Friderichsen syndrome were given cortisone for 10 days.

There were 181 complete recoveries (91%), 12 deaths (6%), and 5 patients with sequelae (3%). Excluding those dying within 24 hours of admission (9 patients), there were 186 survivors out of 189 (98%).

The second group was labelled purulent meningitis. The cerebrospinal fluid was turbid, but no organisms were seen on smears or grown on culture. These cases were assumed to be meningococcal as the meningococcus is difficult to demonstrate particularly when antibiotics have been administered before admission to hospital. Therefore, this group of patients was treated in the same way as meningococcal meningitis. Of 36 patients below the age of 10 years, 33 recovered completely (92%), 3 died (8%), and none had sequelae. No patients died in the first 24 hours, and therefore the survival rate was 92%.

Influenzal meningitis, comprising the third group, was treated with chloromycetin, sulphonamide and streptomycin, with daily intrathecal injections of chloromycetin and streptomycin. Intrathecal therapy continued until the sugar in the cerebrospinal fluid was normal and there were not more than 30 - 40 cells per c.mm.; most of these were lymphocytes. General therapy was given for 1 week longer. Of a total of 23 patients below 10 years of age, there were 16 complete recoveries (70%), 5 deaths (21%), and 2 patients with sequelae (9%). Excluding patients dying within 24 hours of admission, the survival rate was 82%.

In the last group, pneumococcal meningitis, treatment consisted of penicillin, chloromycetin and sulphonamide, with daily intrathecal injections of penicillin and chloromycetin until the cerebrospinal fluid was normal by the same criteria as for influenzal meningitis. Again, general therapy continued for 1 week more. Of 12 patients below the age of 10 years, 11 recovered completely (92%), 1 died (8%) and none had sequelae. The death occurred within 24 hours of admission, and therefore, excluding this patient, the survival rate was 100%.

It was also found that the average duration of history before admission to hospital was longer in patients who died or were left with sequelae.

The conclusion drawn was that failure to achieve 100% recovery was due to 4 factors: (1) Failure to call for early medical attention; (2) failure of early clinical diagnosis of meningeal irritation; (3) inadequate laboratory facilities for accurate and rapid identification of the aetiologic agent; and (4) lack of the necessary discrimination in selection and use of therapeutic agents.

A COMPARATIVE STUDY OF BIOCHEMICAL INDICES USED IN EVALUATING DIETARY PROTEIN IN YOUNG CHILDREN*

H. E. SCHENDEL, J. D. L. HANSEN, AND J. F. BROCK

Departments of Medicine and Child Health, University of Cape Town

Various biochemical indices have been suggested for use in the diagnosis or assessment of relative protein deficiency. Such indices are also essential for measuring the response of infants with kwashiorkor to various forms of treatment. Most workers have agreed that concentration of albumin in the serum is probably the most satisfactory single index of deficiency or response to treatment. In the present study† we attempted to define numerical ranges in serum-albumin concentration which might be associated with different states of protein nutrition. We also compared changes in albumin concentration with changes in the concentration of 2 other serum constituents in infants receiving various sources of dietary protein both in the ward and under field conditions.

Protein Nutritional Status and the Related Serum-albumin Concentrations

According to our experience of the treatment of infants with kwashiorkor, the concentration of albumin in the serum increases for several weeks and then reaches a plateau. Conversely, when a well-nourished infant receives an inadequate protein diet, the concentration of serum albumin eventually begins to fall until signs of acute deficiency appear. Presumably there might be definite numerical ranges in serum-albumin concentration which could be associated with these phases. We have attempted to define these ranges using data from 160 subjects in various states of protein nutrition. The mean concentration (plus and minus one standard deviation) of serum albumin is respectively, during acute deficiency 1·80 (1·31 - 2·29) g./100 ml.; during marginal protein nutritional status 3·15 (2·78 - 3·52) g./100 ml.; and after repletion 3·84 (3·50 - 4·18) g./100 ml. Obviously such ranges will depend on the particular method and laboratory used in accumulating the data. We have used the biuret method with a 27% sodium sulphate solution at 37°C to precipitate the globulins and standardized with Kjeldahl estimations of serum nitrogen.

Comparison of Dietary Proteins

We tested the correlation of serum albumin on serum-cholinesterase concentrations in another series of 127 subjects at various stages in repletion. This correlation was found to be statistically significant. The concentrations of these 2 biochemical indices were used to compare 80 infants in various states of protein nutrition and to measure their response to milk, mixed, and various vegetable-protein diets. Twelve of these 14 diet comparisons were shown to be statistically different using change in serum albumin as the sole criterion. Seven of these 14 comparisons were found to be statistically different using change in serum cholinesterase as the criterion.

These 2 biochemical indices plus changes in serum-cholesterol concentrations were also used to compare 2 diets which contained the same quality and quantity of fat. The study was a controlled field trial at an orphanage and compared the supplementary effects of lysine and glycine on a basic wheat diet.[1] Statistical differences were found in 3 of the 4 experimental periods when the change in serum-albumin concentration was used as the criterion; 4 were found different when the change in serum cholinesterase was used and 2 were found different when the change in serum-cholesterol concentration was used as the criterion.

SUMMARY

Numerical boundaries for serum-albumin concentration have been described for infants at 3 stages of protein nutrition: acute deficiency, 1·31 - 2·29; marginal protein nutritional status, 2·78 - 3·52; and repletion, 3·50 - 4·18 g./100 ml. Changes in the concentration of serum cholinesterase and cholesterol (where the diets contained the same quality and quantity of fat) appear to be useful criteria for the evaluation of dietary proteins and support the conclusions based on changes in the concentration of serum albumin and in body weight.

REFERENCE

1. Krut, L. H.: Unpublished data.

* Abstract of a paper presented at Research Forum, University of Cape Town, 18 May 1960.

† This study was part of the programme of the Clinical Nutrition Research Unit supported in the Department of Medicine by grants from the South African Council for Scientific and Industrial Research; the Williams Waterman Fund for the Combat of Dietary Diseases, Research Corporation, New York, USA; the Food and Nutrition Board, National Research Council, USA; and the Archibald R. Richardson Research Fund, Cape Town.

DAILY PARTITION OF URINARY NITROGEN AND NITROGEN BALANCE DURING TREATMENT OF PROTEIN-DEPLETED INFANTS*

H. E. SCHENDEL and J. D. L. HANSEN, *Departments of Medicine and Child Health, University of Cape Town*

Urinary nitrogen was first partitioned into 5 components in 1905 by Otto Folin.[1,2] From this early study of a human subject maintained on a constant diet for 1 week, Folin derived his concept that nitrogen metabolism was made up of exogenous and endogenous aspects. Greater understanding of methodology and an intense interest in the metabolism of various syndromes have made similar investigations under various conditions periodically necessary and informative. The purpose of the present investigation† is to correlate nutritional status with changes in various urinary nitrogenous constituents.

Partition of urinary nitrogen into 7 components and complete nitrogen balance was conducted daily throughout the repletion of 6 infants with kwashiorkor. After receiving electrolyte therapy for the first 12 - 24 hours, the infants were put on milk diets. Three of them received milk *ad lib.* and 3 received a lesser amount of milk for 10 days, followed by an isonitrogenous substitution of maize. We were unable to distinguish a difference in the urinary constituents when maize was substituted isonitrogenously for milk in these 3 infants as long as we corrected for the difference in absorption. Therefore the diet for these infants has been referred to as a low-protein diet. Urine from a healthy, active child living in a home environment was also collected for 2 weeks and partitioned.

The question as to what is the best expression of particular data is often a very perplexing one. This is especially true when the subjects are heterogeneous by certain criteria and/or are in an especially dynamic state. We have attempted to express our data in such a way as to reflect possible shifts in metabolism which might occur during the repletion of protein-depleted infants.

Urea(mg./absorbed nitrogen/day). The excretion of urea was low in our protein-depleted infants as expected. The effect

* Abstract of a paper presented at Research Forum, University of Cape Town, 18 May 1960.

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of increasing nitrogen intake on urea excretion was also clearly demonstrated. There was a tenfold increase in excretion by infants receiving milk *ad lib.* compared with no change in those receiving the low-protein diet. When the difference in intake as well as absorption was corrected for by using the expression percentage of absorbed nitrogen, the increase in urea excretion with treatment was much more uniform for all 6 of the infants. This twofold increase in urea excretion was probably a better reflection of the increased turnover rate of protein metabolism which would be associated with repletion.

Ammonia(mg./day). There was no apparent change in ammonia excretion by these infants from the second day of hospitalization (after electrolyte therapy) until cure was judged to be initiated.

Amino-acids(mg./mg. urinary creatinine/day; mg./absorbed nitrogen/day). These data clearly demonstrated the development and recession of the increased amino-aciduria which we have previously reported [3,4] during the treatment of infants with kwashiorkor. The effect of nitrogen intake on excretion was confirmed and demonstrated the need for expressing such data as a function of absorbed nitrogen.

Uric acid(mg./day). The excretion of uric acid in both groups increased significantly during repletion.

Creatinine(mg./day). Difference in creatinine excretion between the 2 groups of infants receiving the high and low protein intakes was apparent within 10 days. This difference probably reflected the difference in the rate of accumulation of muscle mass by the 2 groups.

Creatine(mg./day). Creatine excretion increased markedly in the infants receiving milk *ad lib.* The decrease in excretion by 1 of these infants to admission levels occurred several days before signs of a concurrent infection were recorded. Creatine excretion fell uniformly in the infants receiving the low-protein diet.

Undetermined nitrogen(mg./day). The urinary excretion of 'undetermined' nitrogen was understandably irregular since it was estimated by difference and thereby reflected the irregularities and error in the estimation of the 7 other nitrogenous components. There was a significant increase in the absolute excretion by those infants with the high-protein intake.

Nitrogen retention(mg./absorbed nitrogen/day). These observations on continuous nitrogen balance clearly illustrated several of the principles discussed in a recent publication [5] on balance studies conducted in our unit. For example, the mean retention was greater during the first few days of treatment (approximately 65% of absorbed nitrogen) and became less as repletion continued (approximately 20% of absorbed nitrogen after 2 weeks of treatment). It also appeared, in these subjects at least, that the day-to-day variation in nitrogen retention could be accounted for almost entirely on the basis of stage of depletion, and variation in absorption and/or intake.

SUMMARY

Basic data on nitrogen retention and the excretion of various end-products of nitrogen metabolism have been accumulated continuously throughout the treatment of infants with kwashiorkor. These data reflect the degree of protein deficiency in the infants and the quantitative differences in the dietary protein and/or absorption. Qualitative differences in dietary protein however, were not demonstrated in this series.

REFERENCES

1. Folin, O. (1905): Amer. J. Physiol., **13**, 45.
2. *Idem* (1905): *Ibid.*, **13**, 65.
3. Schendel, H. E., Antonis, A. and Hansen, J. D. L. (1959): Pediatrics, **23**, 662.
4. Schendel, H. E. and Hansen, J. D. L. (1959): S. Afr. Med. J., **33**, 871.
5. Hansen, J. D. L., Schendel, H. E., Wilkens, J. A. and Brock, J. F. (1960): Pediatrics, **25**, 258.

ABSTRACT : UITTREKSEL *

UNSATURATED FATS IN FOODS

As a result of the recent practice of advertising the presence of unsaturated fats in foods, the Food and Drug Administration of the United States of America has declared, in its Federal Register, that any claim, direct or implied (in the labelling of fats and oils or other fatty substances offered to the general public) that these substances will prevent, mitigate, or cure diseases of the heart or arteries, is false or misleading and constitutes misbranding within the meaning of the Federal Food, Drug, and Cosmetic Act.

The FDA states that the rôle of cholesterol in heart and artery diseases has not been established; that a causal relationship between blood-cholesterol levels and those diseases has not been proved; and that it has not been demonstrated that it is advisable for Americans to make extensive changes in the nature of the fat they eat.

* From *British Food Journal and Hygienic Review*, vol. 62, p. 77, July 1960.

ASSOCIATION NEWS : VERENIGINGSNUUS

CAPE WESTERN BRANCH

A circular letter from the Hon. Secretary of this Branch is reproduced below for the information of members of the Association:

CHEQUES FROM THE SOUTH AFRICAN MUTUAL MEDICAL AID SOCIETY

I wish to draw the attention of members to a new form of cheque being used by the above Society, and particularly to column 1 of the cheque which is titled 'Payment Codes'. This payment code reads from 1 - 8.

The wording of Code 4/5 is such that the cheque value is according to the Medical Aid Tariff and is tendered in 'full settlement' of the gross amount of the account.

If members are not prepared to accept this, Branch Council recommends that cheques coded 4/5 be returned with the request that they be re-coded to 6, which reads:

> 'Attached is a cheque payable to you. The amount of the cheque represents the benefit payable by the Society on the account detailed hereon.'

Any balance between the cheque value and the full account can then be claimed from the patient.

TAK WES-KAAPLAND

'n Omsendbrief van die Eresekretaris van hierdie tak word hier weergegee ter inligting van lede van die Vereniging:

TJEKS VAN DIE SUID-AFRIKAANSE ONDERLINGE MEDIESE HULPVERENIGING

Ek wil die aandag van lede vestig op 'n nuwe soort tjek wat deur die bogenoemde vereniging gebruik word, veral op die eerste kolom van die tjek onder die hoof ‚Betalingskodes'. Die betalingskode lees van 1 - 8.

Die bewoording van kode 4/5 is so dat die waarde van die tjek gebaseer is op die mediese hulptarief en dat dit aangebied word as ‚volle vereffening' van die totale bedrag van die rekening.

Indien lede nie gewillig is om vereffening op hierdie manier te aanvaar nie, beveel die Takraad aan dat tjeks wat in terme van kode 4/5 uitbetaal word, teruggestuur word met die versoek dat hulle oor-uitgemaak word in terme van kode 6 wat soos volg lees:

> ‚Aangeheg is 'n tjek ten gunste van uself. Die bedrag van die tjek verteenwoordig die voordeel deur die Vereniging betaalbaar op die rekening hierop uiteengesit.'

Die verskil tussen die waarde van die tjek en die volle rekening kan dan van die pasiënt ge-eis word.

PHARMACEUTICAL NEWS : FARMASEUTIESE NUUS

THE WELLCOME TRUST : NEW CHAIRMAN

Since the death of Sir Henry Wellcome in 1936 the trustees of his will have been operating as the Wellcome Trust. Sir Henry Dale, *O.M., G.B.E.*, M.D., F.R.C.P., F.R.S., the senior trustee, has served as Chairman of the Trust for the last 22 years. Having now reached the age of 85 he has retired from the Trusteeship, but he has accepted the invitation of the Wellcome trustees to retain his connection with their activities in an advisory capacity. The Right Hon. Lord Piercy, *C.B.E.* has succeeded him as Chairman.

WESTDENE PRODUCTS (PTY.) LTD.

Westdene Products (Pty.) Ltd. have announced their appointment as sole South African agents for Astra International of Sweden.

Astra was founded in 1913 and since then it has developed steadily year by year until today it is one of the largest pharmaceutical houses in Europe. More than 2,200 people are employed in its Swedish factories and in the 14 subsidiary companies in various parts of the world. Almost 250 of these employees are actively engaged in research projects covering pharmaceutical preparations, surgical instruments, agricultural and chemical industrial products, etc. Astra's present manufacturing programme covers no less than 400 different products.

The best known of the many products which have been discovered in the Astra Research Laboratories is, of course, xylocaine — the original lignocaine which is still regarded by many as the finest local anaesthetic available. However, many more products of original research from the Astra Laboratories will be reaching South Africa during the coming months as a result of the new link with Westdene's Ethical Division. Details regarding these products will be announced as soon as they become available.

PASSING EVENTS : IN DIE VERBYGAAN

Santam-Sanlam Sick Fund. The attention of members of the Medical Association is drawn to the advertisement of the Santam-Sanlam Sick Fund which appeared in the issue of the *Journal* for 6 August.

In order to avoid unnecessary enquiries and correspondence later, members are advised to make sure that all accounts for the treatment of members of the Fund up to 30 June 1960 are submitted to the Fund before the closing date (30 September).

* * *

Members are reminded that they should notify any change of address to the Secretary of the Medical Association of South Africa at P.O. Box 643, Cape Town, as well as to the Registrar of the South African Medical and Dental Council, P.O. Box 205, Pretoria. Failure to advise the Association will result in non-delivery of the *Journal*. This applies to members proceeding overseas as well as those who change their addresses within the Union.

* * *

South African Institute for Medical Research, Johannesburg, Staff Scientific Meeting. The next meeting will be held on Monday 19 September at 5.10 p.m. in the Institute Lecture Theatre. Dr. R. Dorfman will speak on 'The rôle of enzyme histochemistry in pathology'.

* * *

University of Cape Town and Association of Surgeons of South Africa (M.A.S.A.), Joint Lectures. The next lecture in this series will be held on Wednesday 14 September at 5.30 p.m. in the E-floor Lecture Theatre, Groote Schuur Hospital, Observatory, Cape. Prof. J. H. Louw will speak on 'Aorto-iliac occlusive disease'. All members of the Medical Association are welcome to attend this lecture.

* * *

Southern African Cardiac Society. This Society will hold a Cardiac Symposium in Cape Town, at the Department of Medicine, University of Cape Town, Medical School, Observatory, from Wednesday 19 October at 2.30 p.m. to Saturday 22 October at 12 noon. Members of the Society, who have not yet signified their intention of attending the Symposium, are urged to do so immediately to: 'Cardiac Congress', 903 Medical Centre, Heerengracht, Cape Town.

* * *

Southern Transvaal Branch (M.A.S.A.). The monthly general meeting of this Branch will be held at Medical House, 5 Esselen Street, Hospital Hill, Johannesburg, on Tuesday 20 September at 8.15 p.m. Mr. F. W. Holdsworth, President-elect of the British Orthopaedic Association and one of the leading orthopaedic surgeons in Britain, will address the meeting on 'The aetiology and prevention of deformities in poliomyelitis'.

* * *

Western Cape Marriage Guidance Council. A symposium on 'Marriage guidance' will be held on Wednesday 14 September at 8.15 p.m. in the Physiology Lecture Theatre, Medical School, Observatory, Cape (telephone 55-2455). This symposium is organized for medical practitioners only and all doctors are welcome to attend. Speakers will include Dr. W. D. Marais, snr., Dr. D. J. Steenkamp and Mrs. J. Louw. Practitioners will be able to meet the counsellors, see what form the counselling takes, and learn what type of cases are handled. The Council hopes, by this symposium, to be able to prevent any misconceptions arising in the minds of doctors concerning the work of this body.

* * *

Dr. Cecil Morris, orthopaedic surgeon, of Johannesburg, is at present on a visit to the USA where he attended the Eighth World Congress of the International Society for the Welfare of Cripples on 28 August - 2 September and the Eighth Congress of the International Society of Orthopedic Surgery and Traumatology (SICOT) on 4 - 10 September in New York. Dr. Morris will visit a number of orthopaedic centres in the USA before returning to the Union.

* * *

Dr. Noel H. Aldridge, M.B., Ch.B., D.M.R.D., L.M.C.C., Cert. Rad. (R.C.P. & S. Eng.), formerly Director of the Department of Radiology, St. Joseph's Hospital, Sarnia, Canada, and previously of the Johns Hopkins Hospital, Baltimore, USA, has joined the staff of the Department of Radiology of the Massachusetts General Hospital, and the Harvard Medical School, Boston, USA.

* * *

Dr. David Ordman, of the South African Institute for Medical Research and the Department of Microbiology and Pathology of the University of the Witwatersrand, Johannesburg, is at present in the UK where he attended the Second International Congress of Bioclimatology and Biometeorology in London on 5 - 10 September. Dr. Ordman, who is Secretary of the Committee of Allergic Diseases of the International Society of Bioclimatology and Biometeorology, was Chairman of the specialized working group which dealt with the subject of 'Weather, climate, season and asthma'.

* * *

Dr. H. Lidsky, of Sea Point, Cape Town, left on 4 September to take up an appointment as an anaesthetist at the Beilinson Hospital, Petah Tikvah (Tel Aviv), Israel.

* * *

The Planned Parenthood Association of Natal (W.O. 2139) was founded in Durban 2½ years ago to give advice on family planning. It is affiliated to the National Organization (under the Presidency of Dr. Joan Morrison of Port Elizabeth) and through it to the International Planned Parenthood Federation.

The year's figures of attendance at the Association's 5 clinics in Durban numbered 429 new cases and 471 re-visits. A European clinic has just been opened. The Association is dependent

on voluntary donations and grants-in-aid. Medical and nursing staffs give their services voluntarily. Expenditure amounted to £281.

Non-European parents should be referred to Bolton Hall clinics, 77 Albert Street, on Wednesdays and Saturdays at 9.30 a.m. and on Thursdays at 2.00 p.m. The European clinic is open at 2.00 p.m. on Fridays at Bellhaven, Daly Road, (phone 61911). Fees average 7s. 6d. for non-Europeans and 10s. for Europeans. Volunteers from practitioners would be welcome to run clinic sessions.

SECOND CONGRESS OF THE ASSOCIATION OF SURGEONS OF SOUTH AFRICA (M.A.S.A.), DURBAN, 17 - 20 SEPTEMBER 1960

The Second Congress of the Association of Surgeons of South Africa (M.A.S.A.) will be held at the Medical School, University of Natal, Durban, on 17 - 20 September 1960.

PROGRAMME

Saturday 17 September

The duties and conscience of a surgeon : Mr. A. Radford
Shoulder-arm pain : Mr. W. Girdwood
A new technique in the diagnosis of Hirschsprung's disease : Mr. B. Shandling
Postoperative intestinal obstruction in infancy and childhood : Mr. W. Kark
Intestinal obstruction : Mr. A. Dickson Wright

Buffet luncheon and group discussions

Case demonstrations at the King Edward VIII Hospital
Experiences in the surgery of gastro-intestinal haemorrhage : Mr. G. J. Kane
Thrombosis of major artries treated by thrombo-endarterectomy : Mr. H. Gaylis
Observations in oesophageal surgery : Mr. D. S. Chapman

Evening ceremony to admit Mr. A. Dickson Wright to an Honorary Fellowship of the College of Physicians, Surgeons and Gynaecologists of South Africa

Monday 19 September

Analgesia in biliary pain : Mr. G. Efron
Observations on the aetiology of gallstones : Mr. T. G. Lorentz
Operative cholangiography : Mr. C. A. R. Schulenberg
Biliary surgery : Mr. A. Dickson Wright
The value of sialography in the diagnosis of tumours of the parotid salivary gland : Prof. D. J. du Plessis
Treatment of malignancy by regional perfussion : Mr. I. Barnat
The pathology and treatment of intestinal polyps : Mr. A. Walt
Phagedaenic tropical ulcer : Mr. R. J. Fleming
Hiatus hernia and its surgical treatment : Mr. D. N. Fuller
Surgical aspects of bilharziasis : Prof. A. E. Kark

Tuesday 20 September

A review of the diagnosis and treatment of varicose veins : Mr. R. J. Fleming
Paget's disease of the nipple : Mr. C. Toker
Local recurrence of breast cancer : Mr. P. Helman
Basal-cell epithelioma : Mr. B. W. F. Bishop
Moles and melanomata : Mr. J. Heselson
Aspects of head injuries : Mr. A. D. Muskat

Luncheon with an address by Mr. A. Dickson Wright

Case demonstrations at the Addington Hospital.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

LICARAN

Union Chimique Belge, S.A., introduce Licaran - phenetamine, a spasm-relaxant of smooth muscle, and supply the following information:

Indications

In obstetrics Licaran is used during labour for cervical spasms, incoordinated contractions of uterine body, and uterine hypotonia (in association with oxytocine), and also at the terminal stage of dilation for false labour and for threatening abortions.

Licaran is used in gastro-enterology for spasm and dyskinesia of the bile ducts, post-cholecystectomy syndromes, spastic colitis, and spasmodic constipation.

Comments

Licaran is a spasmolytic of the papaverine type. Its effectiveness extends to a whole range of spasms: intestinal, induced by barium chloride; uterine, induced by pituitrin; and ureteral, induced by prostigmin.

Licaran is supplied in bottels of 20 and 100 50mg. tablets; in boxes of 3 and 25 ampoules, and in boxes of 6 suppositories.

Licaran is distributed by Scherag (Pty.) Ltd., P.O. Box 7539, Johannesburg, from whom further information may be obtained.

LIBRIUM

Roche Products (Pty.) Ltd. announce the introduction of an entirely new psychoregulator with a wide spectrum of activity as yet quite unknown in the field of special and general therapeutics, and supply the following information:

Librium contains methaminodiazepoxide(7-chloro-2-methlyl-amino-5-phenyl-3H-1, 4-benzodiazepine-4-oxide hydrochloride), a colourless crystalline substance highly soluble in water, unstable in solution, and sensitive to light.

Pharmacology. Because of its uniqueness it is difficult to describe Librium with known terminology, but it could best be called a psycholeptic with a broad spectrum.

Librium has a quietening effect, abolishing anxiety, tension, and unreasoned fears. It furthermore produces a degree of muscle relaxation. It is an anti-depressant used in treating endogenous, exogenous, neurotic, and exhaustive types of patients. In animal experiments it showed an unprecedented taming action, changing the general aggressive behaviour-pattern to a marked degree. These effects have never before been found in any other preparation which makes it difficult to compare Librium with the other drugs of psychoregulator groups.

1. *Toxicity.* Acute: The unusually broad margin of safety of Librium was demonstrated in studies on mice and rats. Only sedation was observed in animals receiving a lethal dose, but no hypnosis. Chronic: The results of prolonged administration of Librium confirmed the inherent low toxicity as shown in the acute studies. Ordinary doses as high as 80 mg. per kg. of body weight did not produce emesis or ataxia. Mild somnolence appeared to be the only registerable toxic effect in pre-lethal doses. Administration of Librium up to 40 weeks in sub-lethal doses did not adversely affect general health. No histopathology was found in organs and tissues at postmortem examinations.

2. *Human-tolerance determination.* In doses ranging from 100 to 300 mg. per day no side-effects were seen in 75% of a controlled series. The remaining 25% of patients appeared a little drowsy and mildly ataxic. In a second series of studies up to 500 mg. were given for a period of 8 weeks in chronic incurable schizopherenia. Only 20% of the patients treated showed severe ataxia which disappeared on the reduction of the dosage. There were no significant changes in haematocrit, blood picture, kidney or liver function. The investigation of

blood-plasma levels and urinary-excretion rates of Librium in patients who received 150 mg. daily showed a consistently high blood level after the first 2 days. The therapeutic dose which is suggested varies between 10 and 30 mg. daily on the average.

3. *Excretion.* Approximately 1 - 2% of the daily dose appeared in the urine in the free form and 3 - 6% as a combined excretion product. The drug is mildly accumulative and maximum therapeutic effect is reached within 2 - 3 days. Small amounts of Librium are detectable up to 10 days after a single dose.

4. *Mode of action.* Librium has neuroleptic, psycholeptic, muscle relaxant, anticonvulsant, anti-emetic, spasmolytic, and antidepressive properties. It is also a mild anti-histaminic and is used for potentiation of anaesthesia.

Indications. States of anxiety, tension and restlessness, psychoneuroses, organic neuroses, psychomotor agitation, itching dermatoses, spastic states of striated muscles, sleep disorders, neurotic reaction to organic diseases, relief of stress and strain, removal of the underlying causes and agitated depressions in acute and chronic alcoholism, general states of depression, and autonomic, somatic and sleep disorders.

Side-effects. In therapeutic doses no side-effects were observed.

Compatability. There is no known incompatability with any preparation, but it should not be combined with other psychoregulators.

Dosage. Adults: Mild to moderate symptomatology — 10 mg. 2 - 3 times a day. Severe symptomatology — 20 mg. 2 - 3 times a day. Stress and strain symptomatology — 20 - 25 mg. in a single daily dose to produce the specific psychotherapeutic effect during the day and relaxed sleep during the night, which represents the extraordinary diurnal effect of Librium. The dosage for major psychiatric cases is higher and must be determined from case to case. Up to 300 mg. a day has been used.

Further information may be obtained from Roche Products (Pty.) Ltd., P.O. Box 6158, Johannesburg.

ASCOXAL

Astra International, of Sweden, the inventors of xylocaine, have introduced a new principle in the treatment of diseases of the oral mucous membranes. The active principle is the asc-ox reaction, which occurs between ascorbic acid and sodium percarbonate, with copper ions as catalyst, when an Ascoxal tablet is dissolved in water. This reaction has an antimicrobial and viscosity-reducing effect which is up to 250 times stronger than the effect of the individual constituents of the tablet *per se*.

In contrast to antibiotic therapy, Ascoxal does not disturb the normal balance of the oral microflora nor give rise to resistant strains, nor does it produce any form of allergic phenomena. The asc-ox reaction causes no toxic or locally irritating side-effects.

Ascoxal is indicated in the treatment of acute and chronic gingivitis, stomatitis, and oral mycosis. Prophylactically it is indicated in dental surgery and in orthodontic treatment with corrective appliances. Ascoxal is supplied in boxes containing 24 tablets each individually sealed in foil for protection from moisture.

Further information may be obtained from the sole South African distributors, Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg.

CARVASIN

Wyeth Laboratories (Pty.) Ltd., announce the introduction of Carvasin, a long-acting coronary vasodilator, and supply the following information:

Composition. Each Carvasin tablet contains 10 mg. of isosorbide dinitrate (1, 4, 3, 6-dian-hydrosorbitol - 2, 5-dinitrate).

Action and indications. Carvasin is a long-acting coronary vasodilator of unprecedented effectiveness, indicated for the treatment of angina pectoris.

Carvasin offers the following clinical benefits:

(*a*) Rapid onset of action — patients usually experience benefits within 15 - 30 minutes, about half the time encountered with pentaerythritol tetranitrate.

(*b*) Prolonged action — a single dose produces effects which persist for 4 - 5 hours. Convenient *q.i.d.* dosage, therefore, is highly satisfactory for most patients.

(*c*) Greater effectiveness — Carvasin significantly reduces the number, duration and severity of anginal attacks, and has done this in a manner demonstratively superior to that of pentaerythritol tetranitrate. It should be noted in this connection that the average milligram dosage for Carvasin is approximately half that for PETN.

(*d*) Greater safety — the only side-effect observed to date has been headache, which usually responds to acetylsalicylic acid and abates as therapy continues. Persistent headaches can usually be controlled by reduction in dosage. It should be noted that headache is normally considered an indication of effective pharmacodynamic activity.

Carvasin's toxicity is extremely low — approximately 40 times the therapeutic dose is required to produce symptoms of toxicity.

Administration and dosage. The average dose of Carvasin is 1 tablet (10 mg.) 4 times a day, half an hour before meals and at bedtime. For optimum effect, dosage should be adapted to the needs of each case. The dosage range is 5 mg. - 20 mg.

Contra-indications. Like all nitrates, Carvasin should be given with caution to patients with glaucoma.

Carvasin is supplied in bottles of 50 tablets, 10 mg. per tablet.

Further information may be obtained from Wyeth Laboratories (Pty.) Ltd., P.O. Box 42, Isando, Transvaal.

BOOK REVIEWS : BOEKBESPREKINGS

CORONARY DISEASE

Coronary Heart Disease. By J. W. Gofman, M.D., Ph.D. Pp. xx + 353. 60s. Oxford: Blackwell Scientific Publications. 1959.

The investment of the physician's effort in the prevention of coronary heart disease requires a full understanding of advances in knowledge as well as limitations of that knowledge. Professor Gofman has attempted to satisfy this need by providing and integrating available information related to clinical rather than pathological concepts of the disease. In his opinion the atherogenic index derived from the lipoprotein level and the blood pressure provide independent information and can be utilized to predict the risk of coronary heart disease. Concepts of the influence of family history, age, sex, over-weight, diet, cigarette smoking, occupation, stress, and physical exercise, are developed and are augmented by additional chapters on the relation of diabetes mellitus and the thyroid to coronary heart disease. Finally a programme is suggested for prevention of the disease during its sub-clinical phase by lowering the atherogenic index through dietary and pharmaceutical means.

B.B-S.

YEAR BOOK OF MEDICINE

The Year Book of Medicine, 1959-1960. Edited by P. B. Beeson, M.D.; C. Muschenheim, M.D.; W. B. Castle, M.D.; T. R. Harrison, M.D.; F. J. Ingelfinger, M.D. and P. K. Bondy, M.D. Pp. 733. 110 figures. $8.00. Chicago: Year Book Publishers, Inc. 1959.

The latest edition of the *Year Book of Medicine* maintains the high standard of the previous volumes. Once again papers from the world literature covering most of general medicine are reviewed, research and practical clinical topics receiving equal attention. Research topics range from investigations into the common cold, with reviews of work done in America and Britain, to analysis of the various urinary cortisol metabolites. Important papers by South African investigators in the field of fat matebolism and atherogenesis are fully reported.

Inevitably American publications predominate, but it is gratifying to see that a number of papers from South African journals are included. The Editors have admirably and successfully accomplished their task of selection and review, while their comments in the form of footnotes are always succinct and pointed and add greatly to the value of the book. The Year Book can be regarded as essential reading for every physician, and, indeed, it is strongly recommended to doctors in every branch of medicine. H.M.

INSTITUTIONAL NEUROSIS

Institutional Neurosis. By R. Barton, M.B., M.R.C.P., D.P.M. Pp. 56. 3 figures. 8s. 6d. + 5d. postage. Bristol: John Wright & Sons Ltd. 1959.

This booklet assembles hypotheses that have been postulated by writers mainly in the last 20 years regarding processes associated with diseases which call for prolonged institutional care.

An attempt is made to disentangle the effects of chronic schizophrenic processes and even organic dementias from the 'institutional neuroses'.

The work would form a valuable basis for staff discussion where attempts are being made to modify rigid staff attitudes which, no doubt, play their part in the desocialization of institutionalized patients. This publication is recommended for medical and nursing personnel, as well as social workers, engaged in long-term institutional treatment mainly in mental hospitals but also in hospitals for leprosy and tuberculosis and even prisons, orphanages, and work colonies. A.M.L.

CORRESPONDENCE : BRIEWERUBRIEK

INSTRUCTIONS OF DOCTORS TO DISTRICT NURSES

To the Editor: It has been reported to this Council by their travelling nurse that from time to time district nurses in the employ of child welfare societies are administering injections and distributing sulpha drugs on the verbal instructions of a doctor without any written record.

It has also sometimes happened that the supply of drugs prescribed by a doctor in such cases has not always been fully used and the remaining drugs have been left in the medicine cupboard of the district nurse.

Strict instructions have been issued to district nurses that they must either destroy such surplus supplies or return them to the doctor who has prescribed them.

A booklet has recently been issued by this Council entitled *Approved Medicine List and Responsibilities of Nurses and Midwives; and Cooperation with District Surgeons.* My Council would be glad to supply copies of this booklet for the information of any doctors who may be interested to know the instructions issued by this Council to district nurses in the employ of local child welfare societies.

L. M. MacKenzie
Organizing Secretary
South African National Council for Child Welfare
P.O. Box 8539
Johannesburg
19 August 1960

[This letter is published particularly for the information of district surgeons and others whose practices bring them into contact with district nurses in the employ of child welfare societies. — Editor.]

MEDICAL AID SOCIETIES

To the Editor: To the list of injustices and inconsistencies to which Dr. N. R. Pooler[1] has drawn attention I should like to add one other, and also to urge some urgent and positive action by the Association in connection with the disruptive effects on the practices of members of the Association by the medical aid societies.

Firstly, one is constantly being irritated by the members of medical aid societies who fail to intimate that they are members when they first receive treatment.

In an semi-rural practice medical aid society members are not in the majority — it is therefore impractical to ask every new patient whether they are members of a society. Especially is this so when one is first called to a particular house after hours. Consequently normal rates are charged unless notification of membership of a society has been made. Inevitably, each month a number of accounts are returned with the request that they should be adjusted to Tariff rates. On occasions this only happens after two or three 'accounts rendered' have been sent. It is my custom in these cases to fill in the form on the basis of my normal charges and to notify the society concerned that I was not aware that the patient was one of its members. Invariably this notification is ignored by the society and my charges are reduced to Tariff rates. Though the majority of membership cards which I have seen instruct the member that he must acquaint the doctor with the fact of his membership of the society on first attendance, on no occasion has a member been disciplined by his society or reprimanded for his omission. The additional fact that a society rarely indicates in which particulars an account has been amended makes it increasingly difficult to reconcile my books. Much time is also wasted in looking up the additional information requested by the societies.

A little cooperation on this point would remove a considerable amount of present irritation with the societies and their ways.

My second point concerns the disconcerting effect which the entry of insurance companies into the field of 'medical aid' is having on my relationships with my patients. These relationships have become considerably strained because of the peculiar methods by which the patients were persuaded to become policy holders, and I persuaded to recognize them as such.

It was suggested at first that I would be paid at normal rates for my services to policy holders and that the patient would get a refund, according to his policy, of whatever amount he paid to me. Then came the request for a diagnosis and details of treatment before such refund could be made. This was followed by the statement by a company that my charges were 'in excess of Tariff (01)'. What tariff? I am completely unaware of having personally, or through my membership of the Medical Association, agreed to any tariff concerning insurance company policy holders. The only tariff of which I am aware is that agreed to between the Medical Association and *approved* medical societies which specifically excludes any obligation on my part to apply the rates specified therein to members of non-approved societies.

There is, therefore, no justification whatsoever for the insurance companies to allege that my charges are in excess of a non-existent tariff.

In my waiting room there is a notice which states, *inter alia*, that 'no insurance company has been recognized by the Medical Association' and that 'only members of approved medical aid societies will be treated at Tariff rates'. A list of approved societies is attached to the notice. The notice also specifically states that the contract for service lies between the patient and myself and that the function of the non-approved societies is to indemnify the patient, not to pay the doctor. I therefore claim that in accepting my services the patient concerned has, by implication, accepted my normal charges. A list of basic charges is placed alongside the notice mentioned above. This list has an addendum to the effect that the charges may be modified in certain cases.

I would therefore suggest that the repeated notifications received by my patients that my charges are 'in excess of Tariff' constitute a defamatory action on the part of the insurance companies. Is it not time that the Medical Association should take steps to prevent further incidents of this nature?

As a point of interest, is a non-member of the Association bound in any way to accept the Tariff rates? If not, the insinuation of the insurance companies is even more reprehensible, because they have no knowledge on whether or not I am a member of the Association!

Philip H. Dalgleish, M.B., Ch.B.
P.O. Box 79
Hill Crest, Natal
13 August 1960 (received for publication on 22 August)

1. Correspondence (1960) S. Afr. Med. J., **34**, 680 (6 August).